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(54) Amino acid sequences of anti-idiotypic antibodies against anti-cancer human monoclonal antibody, and dna base sequences encoding those sequences

(57) Amino acid sequences of the H chain and L chain variable regions of mouse monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 against idiotypes of a cancer cell antigen-specific human immunoglobulin CLN/IgG produced by a human/human fused cell strain CLN/SUZ H11, and base sequences of the genes of the variable regions are disclosed.

The above amino acid sequences and the base sequences are useful in medical and pharmaceutical fields such as prophylaxis, treatment and/or diagnosis of human diseases, and/or in pharmacological and/or biochemical fields, etc. such as biochemical reagents, and reagents for purification of biomacromolecules.

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**Description****Detailed Description of the Invention**

- 5 This invention relates to the structure of the variable regions of mouse immunoglobulins against idiotypes of an antigen-specific human immunoglobulin, useful in wide fields, for example in pharmaceutical fields such as prophylaxis, treatment and/or diagnosis of human diseases, and/or in pharmacological and/or biochemical fields such as biochemical reagents and reagents for purification of biomacromolecules.
- 10 More detailedly, this invention relates to the amino acid sequences of the H chain and L chain variable regions of mouse immunoglobulins against idiotypes of a cancer cell antigen-specific human immunoglobulin produced by a human/human fused cell strain CLN/SUZ H11 from a B cell of a patient carrying human cervical carcinoma and a human lymphoblastoid cell strain, and relates to the base sequences of the genes of the variable regions.

15 Since the development of the technique of formation of monoclonal antibodies by cell fusion or immortalization of cells, many useful antibodies have been obtained using mainly mice. Among them, monoclonal antibodies against malignant tumor cells are utilized not only for fundamental researches such as analyses of tumor antigens, but in serum diagnoses, image diagnoses of tumors using labeled antibodies, and have extremely high utilization value. Particularly, human-derived anti-cancer monoclonal antibodies are expected as ideal antibodies in the clinical field, since they have only faint or no side effects.

20 In such circumstances, one of the present inventors, as disclosed detailedly in Japanese Laid-Open Patent Publication No. 201994/1983 (= U. S. Patent No. 5,286,647; EP-A-839,02157.3), Japanese Laid-Open Patent Publication N . 135898/1984 and Japanese Laid-Open Patent Publication No. 137497/1984, established a cell strain CLN/SUS H11 (ATCC No. HB 8307) which produces a human monoclonal antibody having a high reactivity with human cancer cells. Interesting findings are obtained about the antibody (named CLN-IgG) produced by this cell strain, that the antibody class is IgG; the isotypes are  $\gamma 1$  type and  $\kappa$  type; and the antibody binds to a cancer antigen immunohistologically existing 25 on the surface of the cancer cells and moreover inhibits proliferation of the cancer cells. At present, the whole amino acid sequence and DNA base sequence of the antibody are clarified (Japanese Laid-Open Patent Publication No. 346792/1992 = WO 92/20799).

30 On the other hand, since Jerne put forward the so-called network theory, various researches have been made on the structure of the variable regions of antibodies. An antibody binds to an antigen at its variable region (antigen combining site). Therefore, the variable regions of antibodies have various three-dimensional-like structures in accordance with the structures of the antigenic determinants on the surfaces of antigens to be recognized. Thus, an antibody itself can be considered to be an antigen, and in the case, the structures of the variable regions of the antibody are called idiotypes, and antibodies against the idiotypes of the antibody are called anti-idiotypic antibodies. The structure corresponding to an antigenic determinant is called an idiotope. An idiotype can be thought to be an aggregate of idiotypes. It was reported 35 that among anti-idiotypic antibodies (Ab2) against an antibody (Ab1) exist antibodies which competitively inhibit binding of Ab1 to an antigen and have idiotopes analogous to antigens recognized by the antibodies, i.e. antibodies having structures as so-called internal images of the antigen.

In view of the above findings, anti-idiotypic antibodies are expected to be utilized for the purpose of treatment and/or diagnosis of cancers.

40 For example, as for the purpose of cancer treatment, a vaccine therapy using an anti-idiotypic antibody as an antigen is made possible. It is generally difficult to get cancer antigens in large amounts, and it is restricted from a safety aspect and an ethical aspect to directly immunize human beings with cancer cells as antigens. Therefore, these problems can be avoided by performing immunization with an anti-idiotypic antibody in place of an antigen.

45 In a diagnostic aspect, anti-idiotypic antibodies can be utilized to examine the state of immune reactions against cancer cells. Specifically, it serves for early detection of cancers, judgment of therapeutic effects to detect or determine one's antibodies against cancer antigens existing in the blood or humor of cancer patients.

Under such technical background, problems as stated below are underlying to be solved.

50 1) When anti-idiotypic antibodies are utilized as vaccines or diagnostic drugs, it is necessary to provide these antibodies in large amounts and stably. 2) There is a possibility to give more powerful vaccines or diagnostic drugs abounding in functionality by altering or modifying the antibodies.

A method by gene manipulation is considered as a means for solving the above problems, i.e. a means for realizing improvement of production amount of the antibodies and elevation or modification of the activities of the antibodies.

55 For example, in the case of the problem of 1), it can be considered to solve the problem by cloning such an antibody gene, introducing the gene into host cells such as animal cells or *Escherichia coli*, expressing the antibody gene to give a large amount of the antibody, and in the case of the problem of 2), it can be considered to alter such an antibody so as to have stronger immunogenicity by artificially changing the antibody gene, or to design an antibody molecule having a higher vaccinal activity by adding a function which the antibody does not inherently have, for example an enzymatic activity, an immunity induction activity or the like to the antibody molecule or a fragment thereof.

For accomplishment of these purposes, separation of anti-idiotypic antibody genes, and clarification of their structures are necessary. However, there has not so far been known anything at all about the structures of L chains and H chains constituting anti-idiotypic antibodies against idiotypes of CLN-IgG, and the gene structures of the variable regions having a function to specifically bind to idiotypes of CLN-IgG.

5 Thus the main object of this invention is to clarify the gene structures of the L chains and the H chains of anti-CLN-IgG idiotype antibodies.

The present inventors have succeeded in creating hybridomas producing, respectively, five kinds of mouse anti-CLN-IgG idiotype antibodies (Idio 3, Idio 17, Idio 20, Idio 27 and Idio 38) having  $\gamma 1$  and  $\kappa$  isotypes against the idiotypes of CLN-IgG; have separated, from the hybridomas, cDNAs encoding the L chains and H chains of the anti-idiotypic antibodies, respectively; have clarified their DNA base sequences; have determined, based on these sequences; the amino acid sequences of the L chains and H chains of the antibodies, respectively; and have completed this invention.

Thus, according to this invention, are provided an immunoglobulin H chain variable region fragment which contains a hypervariable region CDR1 having an amino acid sequence selected from

15 the following: (1) **Ser Tyr Trp Met His;** and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

20 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

25 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

30 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

35 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

40 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

45 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

50 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

55 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

60 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

65 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

70 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

75 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

80 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

85 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

90 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

95 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

100 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

105 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

110 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

115 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

120 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

125 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

130 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

135 Asn Tyr Trp Met Gln; and/or a sequence having a sequence Asp.Tyr.Tyr Met Asn; and/or a sequence

and a hypervariable region CDR3 having an amino acid sequence selected from

(3) Glu Glu Tyr Asp Tyr Asp  
 5 Thr Leu Asp Tyr;  
 Asp Arg Gly Gly Arg Asp  
 Trp Tyr Phe Asp Val;  
 10 Asp Gly Phe Leu Arg Asp  
 Trp Tyr Phe Asp Val; and  
 Ser Gly Tyr Tyr Gly Ser  
 Phe Val Gly Phe Ala Tyr;  
 15

and DNA and RNA fragments encoding the immunoglobulin H chain variable region fragment.

According to this invention are further provided an immunoglobulin L chain fragment which contains a hypervariable

20 region CDR1 having an amino acid sequence selected from

(1) Tyr Arg Ala Ser Lys Ser Val

Gln Leu His Leu Ala Ile Val

Tyr Met His;

Tyr Arg Ala Ser Lys Ser Val

Ser Thr Ser Gly Tyr Ser Tyr

Met His;

Lys Ala Ser Gln Asp Val Asn

Thr Ala Val Ala; and

Lys Ala Ser Gln Asp Val Thr

35 Thr Asp Val Ala .

40 a hypervariable region CDR2 having an amino acid sequence selected from

(2) Leu Val Ser Asn Leu Glu Ser;

Leu Val Ser Asn Leu Asp Ser; and

45 Ser Ala Ser Tyr Arg Tyr Thr,

50 a hypervariable region CDR3 having an amino acid sequence selected from

55

and a hypervariable region CDR3 having an amino acid sequence selected from

- (3) Gln His Ile Arg Val Ala Tyr
- 5 Thr;
- Gln His Ile Arg Gly Ala Tyr
- 10 Thr;
- Gln His Ile Glu Gly Ala Tyr
- 15 Thr;
- Gln Gln His Tyr Ser Pro Pro
- Leu Thr; and
- Gln Gln His Tyr Ser Thr Ala
- Trp Thr;

20 and DNA and RNA fragments encoding the immunoglobulin L chain variable region fragment.

In this invention, cytoplasmic RNAs were prepared from the five mouse hybridomas, respectively; the RNAs were converted to cDNAs by a reverse transcriptase; the antibody genes were amplified using these cDNAs as templates and using the PCR method; the amplified DNA fragments were integrated into plasmids and cloned; the base sequences of the insertion DNAs of the plasmids purified from Escherichia coli clones isolated were determined, and the amino acid sequences were determined based on the base sequences. These steps are further detailedly described below.

#### [1] Isolation of cytoplasmic RNAs

Each mouse hybridoma is cultured and proliferated in a culture medium, e.g. and RDF or RPMI 1640 medium, containing 5% fetal bovine serum under a suitable condition, e.g. under a condition of 37°C and a carbon dioxide concentration of 5%; the resultant cells are collected by centrifugation; and the cytoplasmic RNA is extracted from the cells by a conventional method, e.g. a method disclosed in 7.12 of Molecular Cloning (2nd edition, edited by Sambrook et al., Cold Spring Harbor Laboratory Press 1989). The resultant cytoplasmic RNA can further be utilized as a template for cDNA synthesis. Specifically in this invention, the cytoplasmic RNAs were extracted from mouse hybridomas No. 3, No. 17, No. 20, No. 27 and No. 33, and provided for synthesis of cDNAs.

#### [2] Synthesis of cDNAs

Using a cytoplasmic RNA obtained in the step of [1] as a template, a single-strand DNA complementary to the mRNA is synthesized in the presence of dATP, dGTP, dTTP and dCTP using, as a primer, an oligo dT corresponding to a poly A, or a synthetic nucleotide having a random sequence, and a reverse transcriptase. In the specific operations in the invention, cDNAs were synthesized using the cytoplasmic RNAs obtained in the step of [1] as templates and a random hexamer as a primer, respectively, and provided for the step of amplification of the antibody genes.

#### [3] Amplification of antibody genes by PCR

PCR reaction is performed in the presence of dATP, dGTR, dTTP, dCTP and Taq polymerase using as a template a single-strand cDNA obtained in the step of [2] and as a primer a sequence of the antibody gene (e.g., a sequence encoding a constant region, a variable region or a leader region of the antibody gene) to amplify the antibody gene. Suitably in the invention, the antibody genes were amplified using as templates the single-strand cDNAs obtained in the step of [2] and using synthetic DNA oligomers corresponding to the sequences of the leader regions and variable regions of the L chains and H chains of the antibodies, respectively.

#### [4] Cloning of PCR-amplified DNA fragments

A PCR-amplified DNA fragment obtained in the step of [3] is, directly or after treatment with restriction enzyme(s), ligated into one of various vectors, for example plasmid vectors such as pUC 18, pCR1000 and pCRTM, phage vectors such as M 13 phage, and phagemid vectors such as pUC 118 and pBluescript SK<sup>+</sup> to prepare a vector containing the insertion fragment. Then, Escherichia coli is transformed with the vector, and a colony of the Escherichia coli containing

the targeted antibody gene fragment is obtained. The purified vector recovered from the *Escherichia coli* is provided as a sample for determination of the DNA base sequence. In the specific operations in the invention; the PCR-amplified DNA fragments obtained in the step of [3] were directly ligated, respectively, into pCR1000 and pCR™ plasmid vector; an *Escherichia coli* INVαF was transformed with each of the resultant plasmids; and the plasmids were purified from the resultant *Escherichia coli* colonies, respectively.

#### [5] Determination of the base sequences and amino acid sequences of the DNAs

The base sequence of the DNA at the insertion site in a plasmid obtained in the step of [4] can be determined using the Maxam-Gilbert method or the Sanger method. In the invention, the pCR1000 or pCR™ plasmid vectors containing the insertion fragments were purified, respectively; their base sequences were determined by the Sanger method; and the amino acid sequences were presumed based on their base sequences, respectively.

Hereafter, this invention is further specifically described below according to examples.

Drawings referred to in Examples are briefly described as follows.

Fig. 1 is a drawing showing isotypes of monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33.

Fig. 2 is a drawing showing the monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 specifically bind to CLN-IgG, and do not bind to other human IgGs.

Fig. 3 is a drawing showing that monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 are competitively inhibiting the binding between CLN-IgG and human matrical carcinoma cell ME-180.

Fig. 4 is a drawing where the amino acid sequences of the H chain variable regions of monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 are notated in parallel according to the Kabat's notation, and the regions of the hypervariable regions CDR1, CDR2 and CDR3 are determined.

Fig. 5 is a drawing where the amino acid sequences of the L chain variable regions of monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 are notated in parallel according to the Kabat's notation, and the regions of the hypervariable regions CDR1, CDR2 and CDR3 are determined.

#### Example 1: Preparation of mouse hybridomas

100 µl of 1 mg/ml human IgG (produced by Cappel) is intraperitoneally injected to a Balb/c mouse on the first day after its birth to prepare a mouse having immunological tolerance to human IgG. Six weeks later, the mouse is immunized as follows with CLN-IgG as an antigen.

CLN-IgG purified from a culture medium of a human/human hybridoma CLN/SUZ H11 (ATCC No. HB8307) according to an ammonium sulfate precipitation method and protein A-affinity chromatography was adjusted to a concentration of 2 µg/µl with physiological saline; an equal amount of complete Freund's adjuvant solution was added, and after mixing and emulsification, 100 µl of the emulsion (corresponding to 100 µg of CLN-IgG) was subcutaneously injected into the immunologically tolerated mouse. Thereafter, similar immunization was repeated 4 to 5 times; the murine spleen was enucleated 4 days after the final immunization and made to be spleen cells, and they were used for the following cell fusion.

A mouse parent cells NS-1 (ATCC TIB-18) and the spleen cells are washed with portions of RPMI 1640 medium not containing serum, respectively, and the both of the cells are mixed and centrifuged. 1 ml of 50% polyethylene glycol (average molecular weight: 4,000) is added dropwise to the resultant precipitate over a period of 1 minute. 10 ml of RPMI 1640 medium is further added over a period of 3 minutes, the mixture is centrifuged at 400 × g for 5 minutes, the precipitate is suspended in 10 ml of RPMI 1640 medium containing 20% fetal bovine serum, and the suspension is spread into a 96-well microplate.

Thereafter, the cells were cultured in HAT medium for 14 to 21 days, transferred to HT medium, and finally cultured in RPMI 1640 medium containing 10% fetal bovine serum.

The antibody titers in the culture supernatants on the wells where proliferation was observed were assayed by an enzyme-labeled antibody technique; hybridoma clones secreting monoclonal antibodies which bind to CLN-IgG but not to human IgG were obtained from the appropriate wells by the limiting dilution method; and these hybridoma clones were named No. 3, No. 17, No. 20, No. 27 and No. 33.

#### Example 2: Determination of isotypes of the mouse antibodies

Isotypes of the antibodies secreted from the 5 mouse hybridomas obtained in Example 1 were determined as follows using a mouse monoclonal antibody isotyping kit (produced by Amersham Co.).

The mouse hybridomas are started to be cultured at a concentration each of  $5 \times 10^4$ /ml in portions of RPMI 1640 medium containing 10% fetal bovine serum, respectively, and 5 days later the culture supernatants are obtained, on stick portions of the typing sticks are placed in test tubes, respectively; 3 ml portions of the culture supernatants 5-fold diluted with TBS-T (Tris-buffered saline (TBS, pH 7.6) containing 0.1% Tween 20) are added thereto respectively; and

the mixtures are incubated at room temperature for 15 minutes. The culture supernatants are discarded, 5 ml portions of TBS-T are added, and the typing sticks are washed at room temperature for 5 minutes. TBS-T was discarded, and the washing was repeated once more. 3 ml portions of a peroxidase-labeled anti-mouse antibody 500-fold diluted with TBS-T are added, and the mixtures are incubated at room temperature for 15 minutes. The typing sticks are washed twice in the same manner as above; 3 ml portions of an enzyme substrate solution (obtained by adding one drop of 30% aqueous hydrogen peroxide to 50 ml of a TBS solution of 4-chloro-1-naphtol) are added; the mixtures are subjected to reaction at room temperature for 15 minutes; and then the sticks are washed with distilled water. The isotypes of the mouse antibodies are determined based on the resultant signals, respectively.

As a result, as shown in Fig. 1, all the isotypes of these antibodies were  $\gamma 1$  and  $\kappa$ .

**Example 3: Examination of specificities of the anti-idiotypic antibodies**

It was examined according to a dot blot technique, using an ECL Western blotting detecting reagent (produced by Amersham Co.), that the mouse anti-CLN-IgG idiotype antibodies specifically bind to CLN-IgG. The process is stated below.

CLN-IgG and human IgG1 (produced by Protagen Co.) were diluted with PBS to concentrations of 50 to 0.2  $\mu$ l/ml, respectively. 2  $\mu$ l portions of the thus prepared samples were spotted on a number of Hybond-ECL nitrocellulose membrane (produced by Amersham Co.), respectively, and after being dried, the nitrocellulose membranes were allowed to stand at room temperature for one hour in PBS-T (0.3% Tween-20-containing PBS), containing 5% skim milk. After being washed with PBS-T, the nitrocellulose membranes were allowed to stand at room temperature for one hour in the culture supernatants (500-fold diluted with PBS-T) of mouse hybridomas No. 3, No. 17, No. 20, No. 27 and No. 33, respectively. After being washed with PBS-T, the nitrocellulose membranes were allowed to stand at room temperature for one hour in portions of a peroxidase-labeled sheep anti-mouse Ig antibody 3,000-fold diluted with PBS-T, respectively. After being washed with PBS-T, the nitrocellulose membranes were subjected to reaction for one minute in portions of the ECL detecting reagent, and sheets of X-ray film were exposed for 30 seconds to the light emitted from the resultant nitrocellulose membranes, respectively.

The results of the sheets of X-ray film developed are shown in Fig. 2. Any of the five antibodies bound to CLN-IgG, but did not bind to human IgG1. Namely, it was revealed that these antibodies are specific to CLN-IgG.

Next, it was examined whether or not the mouse antibodies have an activity to inhibit the binding of a human monoclonal antibody CLN-IgG to a human cancer cell. The method is stated below.

A human cervical carcinoma cell ME-180 (available from ATCC) is cultured in DF medium (a 1:1 mixed medium of DME : F-12) containing 10% fetal bovine serum. At the stage when the number of the cells becomes  $5 \times 10^6$  to  $1 \times 10^7$ , the cells are detached from the bottom face of the Petri dish using trypsin, collected by centrifugation and sufficiently washed with the medium. A constant number ( $10^5$ /100  $\mu$ l) each of the cells is placed in each well of a 96-well microtiter plate, and allowed to stand at 37°C overnight to be attached on the plate. 50  $\mu$ l portions of 3% glutaraldehyde solution were added dropwise into the respective wells, and the mixtures are allowed to stand at 37°C for 20 minutes to fix the cells. The cells of each well are centrifuged at 200 x g for 10 minutes and washed three times with a gelatin buffer (10 mM phosphate-buffered physiological saline containing 0.3% gelatin); 200  $\mu$ l portions of 1% bovine serum albumin (BSA) solution are added dropwise; and the mixture is allowed to stand at 37°C for one hour to block the plate. The cells are washed three times with the gelatin buffer to remove BSA not adsorbed. Thereafter, dilutions at various rates (100, to 1,000,000-fold) of the ascites obtained by intraperitoneally inoculating into mice the various hybridomas secreting the mouse anti-idiotypic antibodies are added dropwise together with CLN-IgG (50  $\mu$ g each), and the mixtures are subjected to reaction at 37°C for one hour. The cells of these wells are washed three times with the gelatin buffer. 50  $\mu$ l portions of a 3,000-fold diluted peroxidase-conjugated goat anti-human Ig antibody (produced by TACO Co.) are added dropwise, respectively, and the mixtures are subjected to reaction at 37°C for 30 minutes. The cells are washed three times with the gelatin buffer, and portions of a substrate solution containing hydrogen peroxide and o-phenylenediamine are added to perform reaction in a darkroom. 10 minutes later, 50  $\mu$ l portions of 5N sulfuric acid are added to stop the reaction. When the peroxidase-conjugated goat anti-Ig antibody remains on the microplate, namely when the human IgG to be bound thereto remains, a yellow reaction product having absorption at 490 nm is formed. The amount of CLN-IgG bound to the cancer cell is determined by measuring the amount of the reaction product by a spectrometer.

It was clarified, according to the above method, that all the mouse antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 inhibit the binding of CLN-IgG to the cancer cell (Fig. 3).

From the foregoing, these mouse antibodies are antibodies against the idiotypes of CLN-IgG.

**Example 4: Preparation of RNA**

From the five kinds of mouse hybridomas No. 3, No. 17, No. 20, No. 27 and No. 33, the cytoplasmic RNAs were extracted according to the method disclosed in Molecular Cloning (2nd edition, edited by Sambrook et al., Cold Spring Harbor Laboratory Press 1989) 7, 12, as stated below.

10<sup>8</sup> each of the hybridomas cells are collected by centrifugation, and washed twice with 10 times each precipitate's volume of a phosphate-buffered saline. The cells of these groups are centrifuged at 2,000 x g and 4°C for 5 minutes, and the resultant precipitates are suspended in 200 µl portions of an RNA extracting solution (0.14 M NaCl, 1.5 mM MgCl<sub>2</sub>, 10 mM Tris-HCl pH 8.6, 0.5% Nonidet P-40, 1 mM dithiothreitol, 20 mM vanadylribonucleoside complex), respectively. The suspensions are subjected to vortex for 15 seconds and allowed to stand on ice for 5 minutes. The resultant suspensions are centrifuged at 12,000 x g for 30 seconds to remove the cell nuclei as precipitates; to the supernatants are, respectively, added 200 µl portions of a proteinase buffer (0.2 M Tris-HCl pH 8.0, 25 mM EDTA pH 8.0, 0.3 M NaCl, 1.2% SDS) and 1 µl portions of an aqueous proteinase K solution (20 mg/ml); and the mixtures are sufficiently stirred and subjected to incubation at 37°C for 30 minutes. Equal volume portions of phenol/chloroform are added to the reaction solutions, respectively, and the mixtures are stirred, centrifuged at 5,000 x g and room temperature for 10 minutes, and then allowed to separate into organic layers and aqueous layers, respectively. 400 µl portions of isopropanol cooled on ice in advance are added to the aqueous layers recovered, respectively, and the mixtures are allowed to stand on ice for 30 minutes. The mixtures are centrifuged at 12,000 x g and 4°C for 10 minutes to collect RNAs. The resultant RNA precipitates are washed with 1 ml portions of ethanol, dried under reduced pressure and suspended in appropriate amount portions of TE buffer, respectively. Using the cytoplasmic RNAs obtained according to the above operations, the antibody genes are amplified.

Example 5: Amplification and cloning of the antibody genes by the RT-PCR-method

The antibody genes were amplified from the cytoplasmic RNAs obtained in Example 4, using a GeneAmp® RNA PCR kit (produced by Takara Shuzo Co., Ltd.). First, 20 µl each of reactive solutions were prepared containing PCR buffer II (x1), 5 mM MgCl<sub>2</sub>, 1 mM dATP, 1 mM dGTP, 1 mM dTTP and 1 mM dCTP, 1 U/µl an RNase inhibitor, 2.5 µM a random hexamer, 2.5 U/µl a reverse transcriptase and 100 ng each of the above-mentioned cytoplasmic RNAs, respectively; 20 µl portions of a mineral oil were overlaid thereon respectively; and incubations were performed at room temperature for 10 minutes, at 42°C for 15 minutes, at 99°C for 5 minutes and then at 4°C for 5 minutes to perform cDNA synthesis by reverse transcription reaction. Then, 80 µl portions of a solution consisting of 4 µl of 25 mM MgCl<sub>2</sub>, 8 µl of 10x PCR buffer II, 65.5 µl of sterile distilled water, 0.5 µl of AmpliTaq DNA polymerase (5 U/µl) and 2 µl of PCR primers (each 100 pmoles) were added to the above 20 µl of the reverse transcription reaction solutions; 80 µl portions of the mineral oil were overlaid thereon; and PCR reactions were successively performed. Each reaction was performed by repeating 30 times the cycle of 94°C for 1.5 minutes, 50°C for 2 minutes and then 72°C for 3 minutes. The base sequences of the PCR primers are shown below. The primers contained in a Ig-Prime™ kit (produced by Novagen Co.) were used except for the primer of the leader sequence C for H chains.

Primer for H chains	
Leader sequence A	5' GGGATTCTATGRASTTSKGTYTMARCTKGRTT 3'
Leader sequence B	5' GGGATTCTATGRAATGSASCTGGGTWTYCTCTT 3'
Leader sequence C	5' TTAAATGGTATCCAGTGT 3'
Constant region	5' CCCAAGCTTCCAGGGRCARKGGATARACIGRTGG 3'

Primer for L chains	
Leader sequence A	5' GGGATTCTATGRAGWCACAKWCYCAGGTCTT 3'
Leader sequence B	5' GGGATTCTATGGAGACAGACACACTCCTGCTAT 3'
Constant region	5' CCCAAGCTTACTGGATGGTGGGAAGATGG 3'

In the above, the alphabets other than A, G, C and T mean the following bases. R=A/G, W=A/T, I=inosine, Y=C/T, D=A/G/T, K=G/T, H=A/C/T, S=C/G, V=A/C/G, M=A/C, B=G/C/T

10 µl portions of the resultant 100 µl each of the PCR reaction products are subjected to 1.5% agarose gel electrophoresis, and it was confirmed that the antibody gene fragments each about 600 bp long were amplified. As a result, in the case of the H chains, the antibody genes derived from No. 3 and No. 17 were amplified in the leader sequence A,

the antibody genes derived from No. 20 and No. 27 were amplified in the leader sequence B, and the antibody gene derived from No. 33 was amplified in the leader sequence C. On the other hand, in the L chains, the antibody genes derived from No. 27 and No. 33 were amplified in the case where the leader sequence A was used, and the antibody genes derived from No. 3, No. 17 and No. 20 were amplified in the leader sequence B.

5 Each of the PCR-amplified fragments about 600 bp long was integrated into pCR 1000 vector or pCR™ vector using TA cloning kit (produced by Invitrogen Co.). Specifically, ligation mix solutions were prepared by mixing 1 µl portions of the PCR reaction products, 1:1 µl portions of 10 x the ligation buffer, 2 µl portions of pCR1000 or pCR™ Vector (corresponding to 50 µg), 1 µl of T4 DNA ligase and 6 µl portions of sterilized water, respectively; and incubated overnight at 12°C. Separately, 50 µl portions of a suspension of a competent *Escherichia coli* INVαT strain, to which portions were 10 added 2 µl portions of 0.5 M β-mercaptoethanol, respectively, were prepared; and 1 µl portions of the above ligation mix solutions are added thereto, respectively. The mixtures are allowed to stand on ice for 30 minutes, incubated at 42°C for one minute; and rapidly cooled on ice for 2 minutes. 450 µl portions of SOC medium warmed to 42°C in advance were added to the resultant *Escherichia coli* solutions, respectively, and the mixtures are cultured with shaking at 37°C for one hour. Meanwhile, 25 µl portions of X-Gal (40 mg/ml) are spreaded onto a number of LB agar plates each containing 15 Kanamycin (50 µg/ml), respectively, and the agar plates are incubated at 37°C until each X-Gal completely permeates the agar plate.

200 µl portions of the *Escherichia coli* culture broths after completion of culture were spread on the agar plate dried, respectively, and the plates were allowed to stand at 37°C overnight to give white colonies each having Kanamycin resistance.

20 Plasmids were purified from the *Escherichia coli* clones containing the respective antibody genes, and named 3KB11, 17KB1, 20KB1, 27KA2, 33KA26, 3GB1, 17GB7, 20GA2, 27GA5 and 33GC003, respectively. Purification of the plasmids is performed as follows.

The *Escherichia coli* strains containing the above plasmids, respectively, are cultured 37°C overnight in 100 ml portions of LB medium containing Kanamycin (50 µg/ml), respectively. Each of the resultant culture broths is centrifuged 25 at 3,000 rpm for 10 minutes; the cells collected are suspended in 3 ml of an ice-cooled suspension (50 mM glucose, 10 mM EDTA, 2 mM Tris-HCl pH 8.0); and the suspension is allowed to stand at room temperature for 5 minutes. 6 ml of an alkali lysing solution (0.2 N sodium hydroxide, 1% SDS) is added, and the mixture is mixed by gently turning the centrifugation vessel upside down, and allowed to stand on ice for 5 minutes. 4.5 ml of an ice-cooled neutralizing solution (5 M potassium acetate pH 4.8) is added, and the mixture is centrifuged at 12,000 rpm and 4°C for 10 minutes. The 30 supernatant is transferred into another centrifugation vessel; 1 ml of heat-treated 100 µg/ml RNase A solution is added; and the mixture is subjected to reaction for one hour in an incubator of 37°C to perform RNA digestion. To the reaction solution are added 6 ml of TE buffer-saturated phenol and 6 ml of chloroform/isoamyl alcohol (24:1), and the mixture is subjected to vortex for 30 seconds and then centrifuged at 10,000 rpm and 4°C for 3 minutes. The aqueous layer is transferred into another centrifugation vessel, an equal amount of isopropanol is added, and the mixture is sufficiently mixed and then centrifuged at 10,000 rpm and room temperature for 10 minutes.

The resultant precipitate is washed with 1 ml of 70% cold (-20°C) ethanol, dried under reduced pressure, and dissolved in 480 µl of sterilized water. The solution is transferred into an Eppendorf tube; 120 µl of 4 M NaCl and 600 µl of 13% polyethylene glycol #6900 are added; and the mixture is allowed to stand on ice for 20 minutes. The mixture is then centrifuged at 10,000 rpm and 4°C for 10 minutes, and the precipitate is washed with 1 ml of 70% cold (-20°C) ethanol, 40 dried under reduced pressure and dissolved in 100 µl of TE buffer. The resultant purified plasmid was used as a template for sequencing reaction.

#### Example 6: Determination of the base sequences

45 Sanger reactions were performed using as templates the plasmids cloning purified in Example 5 and a fluorescence-labeled primer; the reaction products were analyzed by a DNA sequencer DSQ-1 (produced by Shimadzu Corporation); and the DNA base sequences of the insert parts of the plasmids were also determined.

The sequencing reactions were performed using AmpliTaq cycle sequencing kit (produced by Takara Shuzo Co., Ltd.) and a fluorescence-labeled primer in a reagent kit (produced by Wakunaga Pharmaceutical Co., Ltd.) exclusively used for a fluorescence-type DNA sequencer. First, 2 to 4 µg of one of the plasmids purified as stated in Example 5 is mixed with 1 µl of the FITC-labeled primer (1 p mole/µl, forward or reverse is used) and 2 µl of the 10 x cycling mix solution, and sterilized water is added to prepare 10 µl in final volume of a reaction mix. Four tubes are prepared in which 2 µl portions of the termination mix (A, G, C, T) were placed in advance, respectively. 2 µl portions of the above reaction mix were taken and placed into the respective tubes. The mixtures are corrected by centrifugation, 10 µl portions of a mineral oil are overlaid, and cycling reactions are performed under the following conditions; Precycle 95°C, 3 minutes; first cycle 95°C 30 seconds, 60°C 30 seconds, 72°C 1 minute (repeated 15 times); second cycle 95°C 30 seconds, 72°C 1 minute (repeated 15 times); postcycle 4°C.

2 µl portions of a reaction-stopping dye solution (95% formaldehyde, 20 mM EDTA, 0.05% methyl violet) are added, and the mixtures are mixed by centrifugation and preserved at 20°C until they are electrophoresed.

As 5% polyacrylamide gel was used one obtained by adding pure water to 30 g of urea, 6 ml of 10 x TBE buffer (0.89 M Tris-HCl, 0.89 M boric acid, 0.025 M EDTA disodium salt) and 10 ml of 30% acrylamide solution (28.5% acrylamide and 1.5% methylenebisacrylamide, both produced by BIO-RAD Co.) to make the whole volume 60 ml; filtering the mixture with 0.22-μm filter; deaerating the filtrate for 30 minutes; adding 150 μl of 10% ammonium persulfate and 15 μl of TEMEO; allowing the mixture to stand overnight to make it gel.

The gel was set in the DNA sequencer DSQ-1, and prerun was performed at a constant voltage of 1,000 V for one hour. Each of the samples was denatured at 95°C for 3 minutes immediately before electrophoresis, and rapidly cooled on ice, and 2 to 3  $\mu$ l of the reaction solution was sucked up from the bottom part of the tube by a micro-syringe and loaded onto the gel. Samples run was performed at a constant electric power of 20 W for 12 hours.

After completion of electrophoresis, the base sequence was determined using the software attached to DSO-1. The sequence was confirmed by sequencing both of the sense and antisense chains of the same plasmid from both directions.

The resultant base sequences of the variable regions of the H chains and L chains of the five kinds of the mouse monoclonal antibodies, and amino acid sequences presumed therefrom are shown in the following sequence listing. Relation between the sequence numbers and the sequences of the clones are as follows:

- 15 Sequence No. 1 : Idio 3 H chain variable region (clone 3GB1)  
Sequence No. 2 : Idio 17 H chain variable region (clone 17GB7)  
Sequence No. 3 : Idio 20 H chain variable region (clone 20GA2)  
Sequence No. 4 : Idio 27 H chain variable region (clone 27GA5)  
Sequence No. 5 : Idio 33 H chain variable region (clone 33GC003)

20 Sequence No. 6 : Idio 3 L chain variable region (clone 3KB11)  
Sequence No. 7 : Idio 17 L chain variable region (clone 17KB1)  
Sequence No. 8 : Idio 20 L chain variable region (clone 20KB1)  
Sequence No. 9 : Idio 27 L chain variable region (clone 27KA2)  
Sequence No. 10 : Idio 33 L chain variable region (clone 33KA26)

#### Example 7 Determination of hypervariable regions

The amino acid sequences obtained in Example 6 were notated in parallel according to the numbering of Kabat et al.'s data base (Sequences of proteins of immunological interest Fifth edition, U. S. Department of health and human services, Public health service, National Institutes of Health, NIH Publication No. 91-3242, Kabat et al. 1991), and the amino acid sequences of the hypervariable regions CDR1, CDR2 and CDR3 of each antibody were identified (Fig. 4, H chains, Fig. 5 L chains). In order to confirm the novelty of the identified amino acid sequences of the hypervariable regions CDR1, CDR2 and CDR3, retrieval by a computer was performed using the above Kabat et al.'s data base and a protein data base NBRF-PDB (National Biomedical Research Foundation - protein data base) Release 36.

As a result, the amino acid sequences of Idio 3 H chain CDR1, Idio 17 H chain CDR1, Idio 20 H chain CDR1, Idio 27 H chain CDR1, Idio 33 H chain CDR2, Idio 3 L chain CDR2, Idio 17 L chain CDR2, Idio 27 L chain CDR2 and Idio 33 L chain CDR2 were the same as those of known antibodies, but the amino acid sequences of other CDRs were

revealed to be novel sequences.

### Sequence Listing

Seq. I.D. number : 1

Sequence length : 399

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

### Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..399

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..27

Characteristics determination method : S

### Sequence

CTG TCG GTA ACT TCA GGG GTC TAC TCA GAG GTT CAG CTC CAG CAG TCT  
Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln Gln Ser

GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC AAG  
Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys Lys

GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA CAG  
Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys Gln

AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA AAT  
Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn

AGT GAT ATT AGC TAC AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG ACT  
Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu Thr

GCC GTC ACA TCC ACC AGC ACT GCC TAC ATG GAA CTC AGA AGC CTG ACA  
Ala Val Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr

AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT TAC  
Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asp Tyr

GAC ACC CTG GAC TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TCC TCA  
Asp Thr Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser

GCC AAA ACG ACA CCC  
Ala Lys Thr Thr Pro

105 110 115 399

120

## Sequence Listing

Seq. I.D. number : 2

Sequence length : 402

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..402

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..30

Characteristics determination method : S

## Sequence (with ST 0 01)

ATT CTG TCG STA ACT TCA GGG GTC TAC TCA GAG GIT CAG CTC CAG CAG	48
Ile Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln Gln	
-10	-5
TCT GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC	96
Ser Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys	
-10	-5
AAG GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA	144
Lys Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys	
-25	-30
CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA	192
Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly	
-40	-45
AAT AGT GAT ATT AGC TAC AGC CAG AAC TTT ARG GAC AGG GCC AAA CTG	240
Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu	
-55	-60
ACT GCC GTC ACA TCC ACC AGC ACT GCC TAC ATG GAA CTC AGA AGC CTG	288
Thr Ala Val Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu	
-70	-75
ACA AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT	336
Thr Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asp	
-80	-90
TAC GAC ACC CTG GAC TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TCC	384
Tyr Asp Thr Leu Asp Tyr Trp Gly Gin Gly Thr Ser Val Thr Val Ser	
-105	-110
TCA GCC AAA ACG ACA CCC	402
Ser Ala Lys Thr Thr Pro	
120	

## Sequence Listing

Seq. I.D. number : 3  
 Sequence length : 438  
 Sequence type : nucleic acid  
 Strandedness : double  
 Topology : linear  
 Sequence kind : mRNA  
 Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..438

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..57

Characteristics determination method : S

## Sequence

ATG GAG TTC GGG CTA AAC TGG GTT TTC CTT GTA ACA CTT TTA AAT GGT	248	
Met Glu Phe Gly Leu Asn Trp Val Phe Leu Val Thr Leu Leu Asn Gly		
15	-10	52
ATC CAG TGT GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG	96	
Ile Gln Cys Glu Val Lys Leu Val Glu Ser Gly Gly Leu Val Gln		
30	1           5           10	10
CCT GGG GGT TCT CTC AGA CTC TCC TGT GCA ACT TCT GGG TTA ACC TTC	144	
Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Leu Thr Phe		
15           20           25	25	
ACT GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GAA CTT	192	
Thr Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Glu Leu		
35           30           35           40	40	
GAA TGG TTG CGT TPF ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA GAC	240	
Glu Trp Leu Gly Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr Asp		
45           50           55           60	60	
TAC AGT GCA TGT GTG AAG GGT CGG TTC ACC ATC TCC AGA GAT AAAT CCC	288	
Tyr Ser Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Pro		
55           60           65           70           75           80	80	
CAA AGC ATC CRC TAT CPT CAA ATG AAC ACC CTG ACC ACT GAG GAC AGT	336	
Gln Ser Ile Leu Tyr Leu Gln Met Asn Thr Leu Thr Glu Asp Ser		
85           90           95           100           105           110	110	
GCC ACT TAT TAG TGT GCA AGA GAT AGG GGG GGG AGG GAC TTG TAC TTC	384	
Ala Thr Tyr Tyr Cys Ala Arg Asp Arg Gly Arg Asp Trp Tyr Phe		
115	120	120
GAT GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA GCC AAA ACG	432	
Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys Thr		
125	130	130
ACA CCC	438	
Thr Pro		

## Sequence Listing

Seq. I.D. number : 4

Sequence length : 411

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..411

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..30

Characteristics determination method : S

## Sequence

CTT GTA ACA CGT TTA AAT GGT ATC CAG TGT GAG GTG AAG CTG GTG GAG  
 Leu Val Thr Arg Leu Asn Gly Ile Gln Cys Glu Val Lys Leu Val Glu  
 -10 -5 1 5 48.

TCT GGA GGA GSC TTG GTA CAG CCT GGG GGT TCT CTG AGA CTC TCC TGT  
 Ser Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys  
 10 15 20 96

GCA ACT TCT GGG TTC ACC TAC ACT GAT TAC TAC ATG AAC TCG GTC CGC  
 Ala Thr Ser Gly Phe Thr Phe Thr Asp Tyr Tyr Met Asn Trp Val Arg  
 25 30 35 44

CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG GGT TTT ATT AGA AAC AAA  
 Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu Gly Phe Ile Arg Asn Lys  
 40 45 50 55 192

GCT AAT TAT TAC ACA ACA GAG TAC AGT GCA TCT GTG AAG GGT CGG TTC  
 Ala Asn Tyr Tyr Thr Glu Tyr Ser Ala Ser Val Lys Gly Arg Phe  
 60 65 70 75 80 240

ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC CTC TAT CTT CAA ATG AAC  
 Thr Ile Ser Arg Asp Asn Ser Gln Ser Ile Leu Tyr Leu Gln Met Asn  
 70 75 80 85 288

ACC CTG AGA GAT GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA GAT GGG  
 Thr Leu Arg Ala Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg Asp Gly  
 90 95 100 105 336

TTC CTA CGG GAC TGG TAC TTC GAT GTC TGG GGC GCA GGG ACC ACG GTC  
 Phe Leu Arg Asp Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val  
 110 115 120 125 384

ACC GTC TCC TCA GCC AAA ACG ACA CCC  
 Thr Val Ser Ser Ala Lys Thr Thr Pro  
 120 125 411

## Sequence Listing

Seq. I.D. number : 5

Sequence length : 363

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : NCDS

Presence position: 1..363

Characteristics determination method : S

## Sequence

GAG	GTT	CAG	CTC	CAG	CAG	TCT	GGG	GCT	CTG	GCA	AGA	CCT	GGG	GCT	48	
Glu	Val	Gln	Leu	Gln	Gln	Ser	Gly	Ala	Glu	Leu	Ala	Arg	Pro	Gly	Ala	
1									10						15	
TCA	GTG	AAC	TTG	TCC	TGC	AAG	GCT	TCT	GGC	TAC	ACC	TTT	ACT	AAC	TAC	96
Ser	Val	Asn	Leu	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Thr	Phe	Thr	Asn	Tyr	
30									20		25		30			
TGG	ATG	CAG	TGG	GT	AAA	CAG	AGG	CGT	GG	CAG	GGT	CTG	GAA	TGG	ATT	144
Trp	Met	Gln	Trp	Val	Lys	Gln	Arg	Pro	Gly	Gln	Gly	Leu	Glu	Trp	Ile	
35									35		40				45	
GGG	GCT	ATT	TAT	CCT	GG	GAT	GGT	GAT	ACT	AGG	TAC	ACT	CAG	AAG	TTC	192
Gly	Ala	Ile	Tyr	Pro	Gly	Asp	Gly	Asp	Thr	Arg	Tyr	Thr	Gln	Lys	Phe	
40									50		55		60			
AAG	GGC	AAG	GCC	ACA	TTG	ACT	GCA	GCT	AAA	TCC	TCC	AGC	ACA	GCC	TAC	240
Lys	Gly	Lys	Ala	Thr	Leu	Thr	Ala	Ala	Ser	Ser	Ser	Ser	Thr	Ala	Tyr	
45									65		70		75			
ATG	CAA	CTC	AGC	AGC	TTG	GCA	TCT	GAG	GAC	TCT	GCG	GTC	TAT	TAC	TGT	288
Met	Gln	Leu	Ser	Ser	Leu	Ala	Ser	Glu	Asp	Ser	Ala	Val	Tyr	Tyr	Cys	
50									80		85		90		95	
GCA	AGA	TCG	GGC	TAC	TAT	GGT	AGC	TTC	GGG	TTT	GCT	TAC	TGG	GGC	336	
Ala	Arg	Ser	Gly	Tyr	Tyr	Gly	Ser	Phe	Val	Gly	Phe	Ala	Tyr	Trp	Gly	
55									100		105		110			
CAA	GGG	ACT	CTG	GTC	ACT	GTC	TCT	GCA								363
Gln	Gly	Thr	Leu	Val	Thr	Val	Ser	Ala								
									115		120					

## Sequence Listing

Seq. I.D. number : 6

Sequence length : 354

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..354

Characteristics determination method : S

## Sequence

GAC ATT GTG CTG ACA CAG TCT CCT GCT TTA GCT GTA TCT CCT CTG	48
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Pro Leu	
1 5 10 15	
GGG CAG AGG GCC ACC ATC TCA TAC ACG GCC AGC AAA AGT GTG CAG TTA	96
Gly Gln Arg Ala Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Gln Leu	
20 25 30	
CAT CTG GCT ATA GTT TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG	144
His Leu Ala Ile Val Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln	
35 40 45	
CCA CCC AGA CTC CTC ATC TAT CTT GTC TCC AAC CTA GAA TCT EGG GTC	192
Pro Pro Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val	
50 55 60	
CCT GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC	240
Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn	
65 70 75	
ATC CAT CCT GTG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC	288
Ile His Pro Val Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Hist	
80 85 90 95	
ATT AGG GTA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA	336
Ile Arg Val Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys	
100 105 110	
CGG GCT GAT GCT GCA CCA	354
Arg Ala Asp Ala Ala Pro	
115	

## Sequence Listing

Seq. I.D. number : 7

Sequence length : 438

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..438

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..39

Characteristics determination method : S

## Sequence

CTA TGG GTA CTG CTG CTC TGG GTC CCA GGT TCC ACT GGT GAC ATT GTG	48				
Leu Trp Val Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Ile Val					
-10	-5	1			
CTG ACA CAG TCT CCT GCT TCA GCT GTA TCT CTG GGG CAG AGG GCC	96				
Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala					
5	10	15			
TCC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAT AGT	144				
Ser Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser					
20	25	30			
TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG CCA CCC AGA CTC CTC	192				
Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln Pro Pro Arg Leu Leu					
35	40	45	50		
ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC CCT GCC AGG TTC AGT	240				
Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val Pro Ala Arg Phe Ser					
55	60	65	70	75	80
GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG	288				
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu					
85	90	95	100	105	110
AGC TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA CGG GCT GAT GCT GCA	336				
Thr Phe Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala Ala					
115	120	125	130	135	
CCA ACT GTA TCC ATC TTC CCA CCA TCC AGT AAG CTT GGG AAA CGG TTC	384				
Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Lys Leu Gly Lys Arg Phe					
GCA CCG					432
Ala Pro					438

## Sequence Listing

Seq. I.D. number : 8

Sequence length : 417

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 28..417

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 28..90

Characteristics determination method : S

## Sequence

GGCCGCG GTGAGAACCG TTGGGAATTC ATG GAG TAC A GAC A CA CTC CTG 48

Met Glu Thr Asp Thr Leu Leu

-20 -15

CTA TGG GTA CTG CTG CTC TGG CTT CCA GGT TCC ACT GGT GAC ATT GTG 96

Leu Trp Val Leu Ile Ile Trp Val Pro Gly Ser Thr Gly Asp Ile Val

-10 -5 1

CIG ACA CAG TCT CCP GCT TCC TTA GCT GTT TCT CTC GGG CGG AGG GCG 144

Leu Thr Glu Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala

5 10 15

ACC ATC TCA TAC AGG GCC AGC AAA AGT GTC ACT ACA TCT GGC TAT AGT 192

Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser

20 25 30

TAT ATG CAC TGG AAC CAA CAG AGA CCA GGA CAG CCA CCC AGA CTC CTC 240

Tyr Met His Trp Asn Gln Gln Arg Pro Gly Gln Pro Pro Arg Leu Leu

35 40 45 50

ATC TAT CTT GTA TCC AAC CTA GAC TCT GGG GTC CCT GCC AGG TTC AGT 288

Ile Tyr Leu Val Ser Asn Leu Asp Ser Gly Val Pro Ala Arg Phe Ser

55 60 65 70

GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCI GTG GAG 336

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu

70 75 80

GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT GAG GGA GCT TAC 384

Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Glu Gly Ala Tyr

85 90 95

ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA 417

Thr Phe Gly Gly Thr Lys Leu Glu Ile Lys

100 105

## Sequence Listing

Seq. I.D. number : 9  
 Sequence length : 420  
 Sequence type : nucleic acid  
 Strandedness : double  
 Topology : linear  
 Sequence kind : mRNA  
 Original source  
 Organism : mouse

## Sequence characteristics

Symbol expressing characteristics :: CDS  
 Presence position : 31..420  
 Characteristics determination method : S  
 Symbol expressing characteristics :: sig peptide  
 Presence position : 31..90  
 Characteristics determination method : S

## Sequence

25	GC GG CG CG GG TG AGA AC CG TT GGG AAT TC ATG GAG ACA CAG TCC CAG	48	
	Met Glu Thr Gln Ser Gln		
	-20	-15	
30	GTC TTT GTA TTC GTG TTT CTC TGG TTG TCT GGT GTT GAC GGA GAC ATT	96	
	Val Phe Val Phe Val Phe Leu Trp Leu Ser Gly Val Asp Gly Asp Ile		
	-10	-5	1
35	G TG ATG ACC CAG TCT CAC AAS AAT TC ATG TCC ACA TCA GTA GGA GAC AGG	144	
	Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly Asp Arg		
	5	10	15
40	GTC AGT ATC ACC TGC AAG GCG AGT CAG GAT GTG AAT ACT GCT GTA GCC	192	
	Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala Val Ala		
	20	25	30
45	TGG TAT CAA CAG AAA CCA GGA CAA TCT CCT AAA CTA CTG CTT TAC TCG	240	
	Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Tyr Ser		
	35	40	45
50	GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT CAC TTC ACT GGC AGT GGA	288	
	Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp His Phe Thr Gly Ser Gly		
	55	60	65
55	TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC AGT GTG CAG GCT GAA GAC	336	
	Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Gly Val Gln Ala Glu Asp		
	70	75	80
60	CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT AGT CCT CCT CTC ACG TTC	384	
	Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Pro Pro Leu Thr Phe		
	85	90	95
65	GGT GCT GGG ACC AAG CTG GAA CTG AAA CGG GCT GAT	420	
	Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala Asp		
	100	105	

## Sequence Listing

Seq. I.D. number : 10

Sequence length : 360

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..360

Characteristics determination method : S

Symbol expressing characteristics : sig\_peptide

Presence position : 1..12

Characteristics determination method : S

## Sequence

GGT GTT GAC GGA GAC ATT GTG ATG ACA CAG TCT CTC AAA TTC ATG TCC  
 Gly Val Asp Gly Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser

1 5 10

ACA TCA GTT GGA GAC AGG GTC ACC ATC ACC TGC AAG GCC AGT CAG GAT  
 Thr Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp

15 20 25

G TG ACT ACT GAT GTA GCC TGG TAT CAA CAG AAA CCA CGA CAA TCT CCT  
 Val Thr Thr Asp Val Ala Trp Tyr Gln Gln Lys Pro Arg Gln Ser Pro

30 35 40

AAA CTA CTG ATT TAC TCG GCA TCC TAT CCG TAC ACT GGA GTC CCT GAT  
 Lys Leu Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp

45 50 55

CGC TTC ACT GGC AGT GGA TCT GGG ACG GAT TTC ACT TTC ACC UATC AGC  
 Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser

60 65 70 75

AGT GTG CAG GCT GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT  
 Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr

80 85 90

AGT ACT GCG TGG ACG TTC GGT GGT GGC ACC AAG CTG GAA ATC AAA CGG  
 Ser Thr Ala Trp Thr Phe Gly Gly Thr Lys Leu Glu Ile Lys Arg

95 100 105

GCT GAT GCT GCA CCA ACT GTA TCC  
 Ala Asp Ala Ala Pro Thr Val Ser

110 115

48

96

144

192

240

288

336

360

## SEQUENCE LISTING

5

## (1) GENERAL INFORMATION:

## (i) APPLICANT:

10

- (A) NAME:HAGIWARA, Yoshihide
- (B) STREET:4-14, Hiraisanso
- (C) CITY:Takarazuka-shi
- (D) STATE:Hyogo-ken
- (E) COUNTRY:Japan
- (F) POSTAL CODE (ZIP):none

15

(ii) TITLE OF INVENTION:AMINO ACID SEQUENCES OF ANTI-IDIOTYPIC ANTIBODIES AGAINST ANTI-CANCER HUMAN MONOCLONAL ANTIBODY, AND DNA BASE SEQUENCES ENCODING THOSE SEQUENCES

20

(iii) NUMBER OF SEQUENCES:48

25

(iv) COMPUTER READABLE FORM:

- (A) MEDIUM TYPE:Floppy disk
- (B) COMPUTER:IBM PC compatible
- (C) OPERATING SYSTEM:MS-DOS 4.0
- (D) SOFTWARE:Microsoft Word, Version 5.5

30

(v) CURRENT APPLICATION DATA:

- (A) APPLICATION NUMBER:EP - 94 115 683,8
- (B) FILING DATE:October 5, 1994

35

## (2) INFORMATION FOR SEQ ID NO: 1:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:5 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:H-CDR1-1
- (D) OTHER INFORMATION:hypervariable region

40

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 1:

Ser Tyr Trp Met His

5

45

## (2) INFORMATION FOR SEQ ID NO: 2:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:5 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

50

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:H-CDR1-2
- (D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 2:

55

Asp Tyr Tyr Met Asn

5

5 (2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:

- (A) NAME/KEY: H-CDR1-3
- (D) OTHER INFORMATION: hypervariable region

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

Asn Tyr Trp Met Gln

5

20 (2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 17 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:

- (A) NAME/KEY: H-CDR2-1
- (D) OTHER INFORMATION: hypervariable region

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

30 Ala Ile Tyr Pro Gly Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys

5

10

15

Asp

35 (2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 19 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:

- (A) NAME/KEY: H-CDR2-2
- (D) OTHER INFORMATION: hypervariable region

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

40 Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Asp Tyr Ser Ala Ser

5

10

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Val Lys Gly

45 (2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 19 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:

- (A) NAME/KEY:H-CDR2-3  
 (D) OTHER INFORMATION:hypervariable region

5 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 6:

Phe Ile Arg Asn Lys Ala Asn Tyr Tyr Thr Thr Glu Tyr Ser Ala Ser  
 5 10 15  
 Val Lys Gly

10 (2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:17 amino acids  
 (B) TYPE:amino acid  
 (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:H-CDR2-4  
 (D) OTHER INFORMATION:hypervariable region

20 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:7:

Ala Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr Thr Glu Lys Phe Lys  
 5 10 15  
 Gly

25 (2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:10 amino acids  
 (B) TYPE:amino acid  
 (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:H-CDR3-1  
 (D) OTHER INFORMATION:hypervariable region

35 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 8:

Glu Glu Tyr Asp Tyr Asp Thr Leu Asp Tyr  
 5 10

(2) INFORMATION FOR SEQ ID NO: 9:

40 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:11 amino acids  
 (B) TYPE:amino acid  
 (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:H-CDR3-2  
 (D) OTHER INFORMATION:hypervariable region

45 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:9:

Asp Arg Gly Gly Arg Asp Trp Tyr Phe Asp Val  
 5 10

50 (2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:11 amino acids  
(B) TYPE:amin acid  
(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

(A) NAME/KEY:H-CDR3-3  
(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 10;

Asp Gly Phe Leu Arg Asp Trp Tyr Phe Asp Val  
5 10

(2) INFORMATION FOR SEQ ID NO: 11:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 12 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:  
(A) NAME/KEY: H-CDR3-4  
(D) OTHER INFORMATION: hypervariable region

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

Ser Gly Tyr Tyr Gly Ser Phe Val Gly Phe Ala Tyr  
5 10

(2) INFORMATION FOR SEQ ID NO: 12:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 17 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:  
(A) NAME/KEY: L-CDR1-1  
(D) OTHER INFORMATION: hypervariable region

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

Tyr Arg Ala Ser Lys Ser Val Gln Leu His Leu Ala Ile Val Tyr Met  
5 10 15  
His

(2) INFORMATION FOR SEQ ID NO: 13:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 16 amino acids  
(B) TYPE: amino acid  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:  
(A) NAME/KEY: L-CDR1-2  
(D) OTHER INFORMATION: hypervariable region

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser Tyr Met His  
5 10 15

## (2) INFORMATION FOR SEQ ID NO: 14:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:11 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

## (ii) MOLECULE TYPE:protein

## (ix) FEATURE:

- (A) NAME/KEY:L-CDR1-3

(D) OTHER INFORMATION:hypervariable region

## (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 14:

Lys Ala Ser Gln Asp Val Asn Thr Ala Val Ala

5

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15

## (2) INFORMATION FOR SEQ ID NO: 15:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:11 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

## (ii) MOLECULE TYPE:protein

## (ix) FEATURE:

- (A) NAME/KEY:L-CDR1-4

(D) OTHER INFORMATION:hypervariable region

## (xi) SEQUENCE DESCRIPTION:SEQ ID NO:15:

Lys Ala Ser Gln Asp Val Thr Thr Asp Val Ala

5

10

30

## (2) INFORMATION FOR SEQ ID NO: 16:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:7 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

## (ii) MOLECULE TYPE:protein

## (ix) FEATURE:

- (A) NAME/KEY:L-CDR2-1

(D) OTHER INFORMATION:hypervariable region

## (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 16:

Leu Val Ser Asn Leu Glu Ser

5

45

## (2) INFORMATION FOR SEQ ID NO: 17:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:7 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

## (ii) MOLECULE TYPE:protein

## (ix) FEATURE:

- (A) NAME/KEY:L-CDR2-2

(D) OTHER INFORMATION:hypervariable region

## (xi) SEQUENCE DESCRIPTION:SEQ ID NO:17:

55

Leu Val Ser Asn Leu Asp Ser

5

5 (2) INFORMATION FOR SEQ ID NO: 18:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH:7 amino acids
  - (B) TYPE:amino acid
  - (C) TOPOLOGY:linear
- (ii) MOLECULE TYPE:protein
- (ix) FEATURE:
  - (A) NAME/KEY:L-CDR2-3
  - (D) OTHER INFORMATION:hypervariable region
- (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 18:

Ser Ala Ser Tyr Arg Tyr Thr

5

20 (2) INFORMATION FOR SEQ ID NO: 19:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH:8 amino acids
  - (B) TYPE:amino acid
  - (D) TOPOLOGY:linear
- (ii) MOLECULE TYPE:protein
- (ix) FEATURE:
  - (A) NAME/KEY:L-CDR3-1
  - (D) OTHER INFORMATION:hypervariable region
- (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 19:

Gln His Ile Arg Val Ala Tyr Thr

5

30 (2) INFORMATION FOR SEQ ID NO: 20:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH:8 amino acids
  - (B) TYPE:amino acid
  - (D) TOPOLOGY:linear
- (ii) MOLECULE TYPE:protein
- (ix) FEATURE:
  - (A) NAME/KEY:L-CDR3-2
  - (D) OTHER INFORMATION:hypervariable region
- (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 20:

Gln His Ile Arg Gly Ala Tyr Thr

5

45 (2) INFORMATION FOR SEQ ID NO: 21:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH:8 amino acids
  - (B) TYPE:amino acid
  - (D) TOPOLOGY:linear
- (ii) MOLECULE TYPE:protein
- (ix) FEATURE:
  - (A) NAME/KEY:L-CDR3-3
  - (D) OTHER INFORMATION:hypervariable region

55

## (xi) SEQUENCE DESCRIPTION:SEQ ID NO:21:

5 Gln His Ile Glu Gly Ala Tyr Thr  
5

## (2) INFORMATION FOR SEQ ID NO: 22:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:9 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

## (ii) MOLECULE TYPE:protein

## (ix) FEATURE:

- (A) NAME/KEY:L-CDR3-4
- (D) OTHER INFORMATION:hypervariable region

## (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 22:

Gln Gln His Tyr Ser Pro Pro Leu Thr  
5

## (2) INFORMATION FOR SEQ ID NO: 23:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:9 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

## (ii) MOLECULE TYPE:protein

## (ix) FEATURE:

- (A) NAME/KEY:L-CDR3-5
- (D) OTHER INFORMATION:hypervariable region

## (xi) SEQUENCE DESCRIPTION:SEQ ID NO:23:

Gln Gln His Tyr Ser Thr Ala Trp Thr  
5

## (2) INFORMATION FOR SEQ ID NO: 24:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:34 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:single
- (D) TOPOLOGY:linear

## (ii) MOLECULE TYPE:cDNA

## (iv) ANTISENSE: no

## (iii) HYPOTHETICAL: no

## (ix) FEATURE:

- (A) NAME/KEY:H Leader Sequence A
- (D) OTHER INFORMATION:R is A or G;

S is C or G; N is T or C;

K is G or T;

Y is C or T;

D is A or G;

M is A or C.

## (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 24:

GGGAATTCAAT GRASTTSKGG YYTMARCTKG RTTT

## (2) INFORMATION FOR SEQ ID NO: 25:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:34 bas pairs  
(B) TYPE:nucl ic acid  
(C) STRANDEDNESS:single  
(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:cDNA  
(iii) HYPOTHETICAL:no  
(iv) ANTISENSE:no  
(ix) FEATURE:  
(A) NAME/KEY:H Leader Sequence B  
(D) OTHER INFORMATION:S is C or G;  
Y is C or T;  
W is A or T;  
R is A or G.

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:25:

**GGGAATTTCAT GRAATGSASC TGGGTYWTYC TCTT**

34

(2) INFORMATION FOR SEQ ID NO: 26:

- (i) SEQUENCE CHARACTERISTICS:

  - (A) LENGTH: 18 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: no

(iv) ANTISENSE: no

(ix) FEATURE:

  - (A) NAME/KEY: H Leader Sequence C

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:

**T<sup>A</sup>TAAATGGTA TCCAGTGT**

18

(2) INFORMATION FOR SEQ ID NO: 27:

- (i) SEQUENCE CHARACTERISTICS:

  - (A) LENGTH: 35 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(iii) HYPOTHETICAL: no

(iv) ANTISENSE: no

(ix) FEATURE:

  - (A) NAME/KEY: H Constant Region
  - (D) OTHER INFORMATION: R is A or G; K is G or T; N is inosine

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27: 67

CCCAAGCTTC CAGGGRCCAR KGGATARACN GRTGG

35

(2) INFORMATION FOR SEQ ID NO: 28:

- (i) SEQUENCE CHARACTERISTICS:

  - (A) LENGTH: 32 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: single
  - (D) TOPOLOGY: linear

- 5           (iii) MOLECULE TYPE: cDNA  
           (iii) HYPOTHETICAL: no  
           (iv) ANTISENSE: no  
           (ix) FEATURE:  
             (A) NAME/KEY: L Lead r Sequence A  
             (D) OTHER INFORMATION: R is A or G;  
                           K is G or T;  
                           W is A or T;  
                           Y is C or T.

10           (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

GGGAATTCCAT GRAGWCACAK WCYCAGGTCT TT

32

15           (2) INFORMATION FOR SEQ ID NO: 29:

- 20           (i) SEQUENCE CHARACTERISTICS:  
             (A) LENGTH: 33 base pairs  
             (B) TYPE: nucleic acid  
             (C) STRANDEDNESS: single  
             (D) TOPOLOGY: linear
- 25           (ii) MOLECULE TYPE: cDNA  
           (iii) HYPOTHETICAL: no  
           (iv) ANTISENSE: no  
           (ix) FEATURE:  
             (A) NAME/KEY: L Leader Sequence B

25           (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

GGAATTCAAT GGAGACAGAC ACACCTCTGC TAT

33

30           (2) INFORMATION FOR SEQ ID NO: 30:

- 35           (i) SEQUENCE CHARACTERISTICS:  
             (A) LENGTH: 30 base pairs  
             (B) TYPE: nucleic acid  
             (C) STRANDEDNESS: single  
             (D) TOPOLOGY: linear
- 40           (ii) MOLECULE TYPE: cDNA  
           (iii) HYPOTHETICAL: no  
           (iv) ANTISENSE: no  
           (ix) FEATURE:  
             (A) NAME/KEY: L constant

40           (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

CCCCAAGCTTA CTGGATGGTG GGAAGATGGA

30

45           (2) INFORMATION FOR SEQ ID NO: 31:

- 50           (i) SEQUENCE CHARACTERISTICS:  
             (A) LENGTH: 357 base pairs  
             (B) TYPE: nucleic acid  
             (C) STRANDEDNESS: double  
             (D) TOPOLOGY: linear
- 55           (ii) MOLECULE TYPE: mRNA  
           (iii) HYPOTHETICAL: no  
           (iv) ANTISENSE: no  
           (vi) ORIGINAL SOURCE:  
             (A) ORGANISM: mouse
- 55           (ix) FEATURE:

(A) NAME/KEY:Idio 3 H chain variable/Idio 17 H chain variable  
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 31:

5 GAG GTT CAG CTC GAG CAG TCT GGG ACT GTG CTG GCA AGG CCT GGG GCT 48  
 Glu Val Gln Leu Gln Ser Gly Thr Val Leu Ala Arg Pro Gly Ala  
 5 10 15

10 TCA GTG AAG ATG TCC TGC AAG GCT TCG GGC TAC ACC TTT AAC AGC TAC 96  
 Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Asn Ser Tyr  
 20 25 30

15 TGG ATG CAC TGG GTA AAA CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT 144  
 Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile  
 35 40 45

20 GGC GCG ATT TAT CCT GGA AAT AGT GAT ATT AGC TAC AGC CAG AAC TTT 192  
 Gly Ala Ile Tyr Pro Gly Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe  
 50 55 60

25 AAG GAC AGG GCC AAA CTG ACT GCC GTC ACA TCC ACC AGC ACT GCC TAC 240  
 Lys Asp Arg Ala Lys Leu Thr Ala Val Thr Ser Thr Ser Thr Ala Tyr  
 65 70 75 80

30 ATG GAA CTC AGA AGC CTG ACA AAT GAG GAC TCT GCG GTC TAT TTC TGT 288  
 Met Glu Leu Arg Ser Leu Thr Asn Glu Asp Ser Ala Val Tyr Phe Cys  
 85 90 95

35 ACA AAA GAG GAA TAT GAT TAC GAC ACC CTG GAC TAC TGG GGT CAA GGA 336  
 Thr Lys Glu Glu Tyr Asp Tyr Asp Thr Leu Asp Tyr Trp Gly Gln Gly  
 100 105 110

40 ACC TCA GTC ACC GTC TCC TCA 357  
 Thr Ser Val Thr Val Ser Ser  
 115

(2) INFORMATION FOR SEQ ID NO: 32:

45 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 366 base pairs.
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:double
- (D) TOPOLOGY:linear

50 (ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

- (A) ORGANISM:mouse

(ix) FEATURE:

- (A) NAME/KEY:Idio 20 H chain variable

55 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 32:

GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG CCT GGG GGT 48  
 Glu Val Lys Leu Val Glu Ser Gly Gly Leu Val Gln Pro Gly Gly  
 5 10 15

60 TCT CTC AGA CTC TCC TGT GCA ACT TCT GGG TTA ACC TTC ACT GAT TAC 96  
 Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Leu Thr Phe Thr Asp Tyr  
 20 25 30

TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GAA CTT GAA TGG TTG 144  
 Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Glu Leu Glu Trp Leu  
 35 40 45

5 GGT TTT ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA GAC TAC AGT GCA 192  
 Gly Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr Asp Tyr Ser Ala  
 50 55 60

10 TCT GTG AAG GGT CGG TTC ACC ATC TCC AGA CAT AAT CCC CAA AGC ATC 240  
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Pro Gln Ser Ile  
 65 70 75 80

15 CTC TAT CTT CAA ATG AAC ACC CTG ACA ACT GAG GAC AGT GCC ACT TAT 288  
 Leu Tyr Leu Gln Met Asn Thr Leu Thr Thr Glu Asp Ser Ala Thr Tyr  
 85 90 95

20 TAC TGT GCA AGA GAT AGG GGG GGG AGG GAC TGG TAC TTC GAT GTC TGG 336  
 Tyr Cys Ala Arg Asp Arg Gly Gly Arg Asp Trp Tyr Phe Asp Val Trp  
 100 105 110

25 GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA 366  
 Gly Ala Gly Thr Thr Val Thr Val Ser Ser  
 115 120

(2) INFORMATION FOR SEQ ID NO: 33:

(1) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 366 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:double
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

(A) ORGANISM:mouse

(ix) FEATURE:

(A) NAME/KEY: Idio 27 H chain variable

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 33:

30 GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG CCT GGG GGT 48  
 Glu Val Lys Leu Val Glu Ser Gly Gly Leu Val Gln Pro Gly Gly  
 5 10 15

40 TCT CTG AGA CTC TCC TGT GCA ACT TCT GGG TTC ACC TTC ACT GAT TAC 96  
 Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Phe Thr Phe Asp Tyr  
 20 25 30

45 TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG 144  
 Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu  
 35 40 45

50 GGT TTT ATT AGA AAC AAA GCT AAT TAT TAC ACA ACA GAG TAC AGT GCA 192  
 Gly Phe Ile Arg Asn Lys Ala Asn Tyr Tyr Thr Glu Tyr Ser Ala  
 50 55 60

55

5 TCT GTG AAG GGT CGG TTC ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC 240  
 S r Val Lys Gly Arg Phe Thr Ile S r Arg Asp Asn S r Gln Ser Ile  
 65 70 75 80

CTC TAT CTT CAA ATG AAC ACC CTG AGA GCT GAG GAC AGT GCC ACT TAT 288  
 Leu Gln Met Asn Thr Leu Thr Arg Ala Glu Asp Ser Ala Thr Tyr  
 85 90 95

10 TAC TGT GCA AGA GAT GGG TTC CTA CGG GAC TGG TAC TTC GAT GTC TGG 336  
 Tyr Cys Ala Arg Asp Gly Phe Leu Arg Asp Trp Tyr Phe Asp Val Trp  
 100 105 110

15 GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA 366  
 Gly Ala Gly Thr Thr Val Thr Val Ser Ser  
 115 120

## (2) INFORMATION FOR SEQ ID NO: 34:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 363 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL: no

(iv) ANTISENSE: no

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: mouse

## (ix) FEATURE:

- (A) NAME/KEY: Idio\_33 H chain variable

## (xi) SEQUENCE DESCRIPTION: SEQ. ID NO: 34:

30 GAG GTT CAG CTC CAG CAG TCT GGG GCT GAA CTG GCA AGA CCT GGG GCT 48  
 Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala  
 5 10 15

35 TCA GTG AAC TTG TCC TGC AAG GCT TCT GGC TAC ACC TTT ACT AAC TAC 96  
 Ser Val Asn Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr  
 20 25 30

40 TGG ATG CAG TGG GTA AAA CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT 144  
 Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile  
 35 40 45

45 GGG GCT ATT TAT CCT GGA GAT GGT GAT ACT AGG TAC ACT CAG AAG TTC 192  
 Gly Ala Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr Thr Gln Lys Phe  
 50 55 60

55 AAG GGC AAG GCC ACA TTG ACT GCA GCT AAA TCC TCC AGC ACA GCC TAC 240  
 Lys Gly Lys Ala Thr Leu Thr Ala Ala Lys Ser Ser Ser Thr Ala Tyr  
 65 70 75 80

50 ATG CAA CTC ACC AGC TTG GCA TCT GAG GAC TCT GCG GTC TAT TAC TGT 288  
 Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys  
 85 90 95

5 GCA AGA TCG GGC TAC TAT GGT AGC TTC GTT GGG TTT GCT TAC TGG GGC 336  
 Ala Arg Ser Gly Tyr Tyr Gly S r Phe Val Gly Phe Ala Tyr Trp Gly  
 100 105 110

CAA GGG ACT CTG GTC ACT GTC TCT GCA 363  
 Gln Gly Thr Leu Val Thr Val Ser Ala  
 115 120

10 (2) INFORMATION FOR SEQ ID NO: 35:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 336 base pairs
  - (B) TYPE:nucleic acid
  - (C) STRANDEDNESS:double
  - (D) TOPOLOGY:linear
- (ii) MOLECULE TYPE:mRNA
- (iii) HYPOTHETICAL:no
- (iv) ANTISENSE:no
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM:mouse
- (ix) FEATURE:
  - (A) NAME/KEY:Idio 3 L chain variable
- (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 35:

25 GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CCT CTG 48  
 Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Pro Leu  
 5 10 15

30 GGG CAG AGG GCC ACC ATC TCA TAC AGG GCC AGC AAA AGT GTG CAG TTA 96  
 Gly Gln Arg Ala Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Gln Leu  
 20 25 30

CAT CTG GCT ATA GTT TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG 144  
 His Leu Ala Ile Val Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln  
 35 40 45

35 CCA CCC AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC 192  
 Pro Pro Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val  
 50 55 60

40 CCT GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC 240  
 Pro Ala Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn  
 65 70 75 80

45 ATC CAT CCT GTG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC 288  
 Ile His Pro Val Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His  
 85 90 95

50 ATT AGG GTA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA 336  
 Ile Arg Val Ala Tyr Thr Phe Gly Gly Thr Lys Leu Glu Ile Lys  
 100 105 110

55 (2) INFORMATION FOR SEQ ID NO: 36:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH: 330 base pairs

- (B) TYPE:nucleic acid
  - (C) STRANDEDNESS:double
  - (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:
  - (A) ORGANISM:mouse

(ix) FEATURE:
  - (A) NAME/KEY:Idio 17 L chain variable

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 36:

GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG 48  
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly

CAG AGG GCC TCC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT  
 Gln Arg Ala Ser Ile Ser Tyr Arg Ala Ser Lys "Ser Val Ser Thr Ser  
 20 25 30

GGC TAT AGT TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG CCA CCC 144  
 Gly Tyr Ser Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln Pro Pro  
 35 40 45

AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC CCT GCC 192  
 Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val Pro Ala  
 50 55 60

AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT 240  
 Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His  
 65 70 75 80

CCT GTG GAG GAG GAT GCT GCA ACC TAT-TAC TGT CAG CAC ATT AGG 288  
 Pro Val Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Arg  
 85 90 95

GGA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA ( )  
 Gly Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
 100 105 110

(2) INFORMATION FOR SEQ ID NO: 37:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 330 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: mRNA

(iii) HYPOTHETICAL: no

(iv) ANTISENSE: no

(vi) ORIGINAL SOURCE:  
(A) ORGANISM: mouse

(ix) FEATURE:  
(A) NAME/KEY: Idio 20 L chain variable

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:

GAC ATT GTG CTG ACA CAG TCT CCT GCT TCA GCT GTA TCT CTG GGG 48  
 Asp Ile Val Leu Thr Gln Ser Pro Ala S r Leu Ala Val Ser Leu Gly  
 5 10 15

CAG AGG GCC ACC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT 96  
 Gln Arg Ala Thr I1 S r Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser  
 20 25 30

10 GGC TAT AGT TAT ATG CAC TGG AAC CAA CAG AGA CCA GGA CAG CCA CCC 144  
 Gly Tyr Ser Tyr Met His Trp Asn Gln Gln Arg Pro Gly Gln Pro Pro  
 35 40 45

15 AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAC TCT GGG GTC CCT GCC 192  
 Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Asp Ser Gly Val Pro Ala  
 50 55 60

20 AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT 240  
 Arg Phe Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His  
 65 70 75 80

25 CCT GTG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT GAG 288  
 Pro Val Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Glu  
 85 90 95

30 GGA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA 330  
 Gly Ala Tyr Thr Phe Gly Gly Thr Lys Leu Glu Ile Lys  
 100 105 110

(2) INFORMATION FOR SEQ ID NO: 38:

30 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 321 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:double
- (D) TOPOLOGY:linear

35 (ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

- (A) ORGANISM:mouse

40 (ix) FEATURE:

- (A) NAME/KEY: Idio 27 L chain variable

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 38:

GAC ATT GTG ATG ACC CAG TCT CAC AAA TTC ATG TCC ACA TCA GTA GGA 48  
 Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly  
 5 10 15

45 GAC AGG GTC AGT ATC ACC TGC AAG GCC AGT CAG GAT GTG AAT ACT GCT 96  
 Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala  
 20 25 30

50 GTA GCC TGG TAT CAA CAG AAA CCA GGA CAA TCT CCT AAA CTA CTG CTT 144  
 Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Leu  
 35 40 45

TAC TCG GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT CAC TTC ACT GGC 192  
 Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp His Phe Thr Gly  
 50 55 60

AGT GGA TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC GGT GTG CAG GCT 240  
 Ser Gly Ser Gly Thr Asp Phe Thr Ph Thr Ile Ser Gly Val Gln Ala  
 65 70 75 80

GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT AGT CCT CCT CTC 288  
 Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Pro Pro Leu  
 85 90 95

ACG TTC GGT GCT GGG ACC AAG CTG GAA CTG AAA 321  
 Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys  
 100 105

## (2) INFORMATION FOR SEQ ID NO: 39:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 321 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:double
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

- (A) ORGANISM:mouse

## (ix) FEATURE:

- (A) NAME/KEY: Idfo\_33\_L chain variable

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 39:

GAC ATT GTG ATG ACA CAG TCT CAC AAA TTC ATG TCC ACA TCA GTT GGA 48  
 Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly  
 5 10 15

GAC AGG GTC ACC ATC ACC TCC AAG CCC AGT CAG GAT GTG ACT ACT GAT 96  
 Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Thr Thr Asp  
 20 25 30

GTA GCC TGG TAT CAA CAG AAA CCA CGA CAA TCT CCT AAA CTA CTG ATT 144  
 Val Ala Trp Tyr Gln Gln Lys Pro Arg Gln Ser Pro Lys Leu Leu Ile  
 35 40 45

TAC TCG GCA TCC TAT CGG TAC ACT GGA GTC CCT GAT CGC TTC ACT GGC 192  
 Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly  
 50 55 60

AGT GGA TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC AGT GTG CAG GCT 240  
 Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Val Gln Ala  
 65 70 75 80

GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT AGT ACT GCG TGG 288  
 Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Thr Ala Trp  
 85 90 95

5           ACG TTC GGT GGT GGC ACC AAG CTG GAA ATC AAA  
       Thr Phe Gly Gly Thr Lys Leu Glu Ile Lys  
       100                                   105

321

## (2) INFORMATION FOR SEQ ID NO: 40:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 399 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:double
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

(A) ORGANISM:mouse

## (ix) FEATURE:

(A) NAME/KEY:Clone 3GB1

## (xi) SEQUENCE DESCRIPTION:SEQ ID NO:40:

CTG TCG GTA ACT TCA GGG GTC TAC TCA GAG GTT CAG CTC GAG CAG TCT   48  
  Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln Gln Ser  
  -5   1                                   5

25           GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC AAG   96  
  Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys Lys  
  10   15                                   20

30           GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA CAG   144  
  Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys Gln  
  25   30                                   35

35           AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA AAT   192  
  Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn  
  40   45                                   50                                   55

40           AGT GAT ATT AGC TAC AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG ACT   240  
  Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu Thr  
  60   65                                   70

45           GCC GTC ACA TCC ACC AGC ACT GCC TAC ATG GAA CTC AGA AGC CTG ACA   288  
  Ala Val Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr  
  75   80                                   85

50           AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT TAC   336  
  Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asp Tyr  
  90   95                                   100

55           GAC ACC CTG GAC TAC TGG GGT CAR GGA ACC TCA GTC ACC GTC TCC TCA   384  
  Asp Thr Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser  
  105   110                                   115

60           GCC AAA ACG ACA CCC   399  
  Ala Lys Thr Thr Pro  
  120

## (2) INFORMATION FOR SEQ ID NO: 41:

## 5 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 402 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:doub
- (D) TOPOLOGY:linear

10 (ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

- (A) ORGANISM:mouse

## (ix) FEATURE:

- (A) NAME/KEY:Clone 17GB7

## (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 41:

ATT GTG TCG GTA ACT TCA GGG GTC TCA GAG GTT CAG CTC GAG CAG 48  
 Ile Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln  
 -10 -5 1 5

TCT GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC 96  
 Ser Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys  
 10 15 20

AAG GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA 144  
 Lys Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys  
 25 30 35

CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA 192  
 Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly  
 40 45 50

AAT AGT GAT ATT AGC TAC AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG 240  
 Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu  
 55 60 65 70

ACT GCC GTC ACA TCC ACC AGC ACT GGC TAC ATG GAA CTC AGA ACC CTG 288  
 Thr Ala Val Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu  
 75 80 85

ACA AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT 336  
 Thr Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asp  
 90 95 100

TAC GAC ACC CTG GAC TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TCC 384  
 Tyr Asp Thr Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser  
 105 110 115

TCA GCC AAA ACG ACA CCC 402  
 Ser Ala Lys Thr Thr Pro  
 120

## 50 (2) INFORMATION FOR SEQ ID NO: 42:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 438 base pairs
- (B) TYPE:nucleic acid

(C) STRANDEDNESS:double  
(D) TOPOLOGY:linear  
(ii) MOLECULE TYPE:mRNA  
(iii) HYPOTHETICAL:no  
(iv) ANTISENSE:no  
(vi) ORIGINAL SOURCE:  
      (A) ORGANISM:mouse  
(ix) FEATURE:  
      (A) NAME/KEY:Clone 20GA2  
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:42:

ATG GAG TTC GGG CTA AAC TGG GTT TTC CTT GTA ACA CTT TTA-AAT GGT : 48  
 Met Glu Phe Gly Leu Asn Trp Val Phe Leu Val Thr Leu Leu Asn Gly  
 -15 . -10 . -5

ATC CAG TGT GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG 96  
 Ile Gin Cys Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Gln  
           1              5              10

CCT GGG GGT TCT CTC AGA CTC TCC TGT GCA ACT TCT GGG TTA ACC TTC 144  
 Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Leu Thr Phe  
 15 20 25

ACT GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GAA CTT 192  
 Thr Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Glu Leu  
 30 35 40 45

GAA TGG TTG GGT TTT ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA GAC 240  
 Glu Trp Leu Gly Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr Asp  
 50 55 60

TAC AGT GCA TCT GTG AAG GGT CGG TTC ACC ATC TCC AGA CAT AAT CCC - 288  
 Tyr Ser Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Pro  
           65               70               75

CAA AGC ATC CTC TAT CTT CAA ATG AAC ACC CTG ACA ACT GAG GAC AGT 336  
 Gln Ser Ile Leu Tyr Leu Gln Met Asn Thr Leu Thr Thr Glu Asp Ser  
           80          85          90

GCC ACT TAT TAC TGT GCA AGA GAT AGG GGG GGG AGG GAC TGG TAC TTC 384  
 Ala Thr Tyr Tyr Cys Ala Arg Asp Arg Gly Gly Arg Asp Trp Tyr Phe  
 95 100 105

GAT GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA GCC AAA ACG 432  
Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys Thr  
110 115 120 125

**ACA CCC** **Thr Pro** 438

(2) INFORMATION FOR SEQ ID NO: 43:

- (i) SEQUENCE CHARACTERISTICS:

  - (A) LENGTH: 411 base pairs
  - (B) TYPE: nucleic acid
  - (C) STRANDEDNESS: double
  - (D) TOPOLOGY: linear

- (iii) MOLECULE TYPE:mRNA  
(iii) HYPOTHETICAL:no  
(iv) ANTISENSE:no  
(vi) ORIGINAL SOURCE:  
          (A) ORGANISM:mous  
(ix) FEATURE:  
          (A) NAME/KEY:Clone 27GA5  
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 43:

CTT GTA ACA CGT TTA AAT GGT ATC CAG TGT GAG GTG AAG CTG GTG GAG 48  
 Leu Val Thr Arg Leu Asn Gly Ile Gln Cys Glu Val Lys Leu Val Glu  
 -10 -5 1 5

TCT GGA GGA GGC TTG GTA CAG CCT GGG GGT TCT CTG AGA CTC TCC TGT 96  
 Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys  
 10 15 20

GCA ACT TCT GGG TTC ACC TTC ACT GAT TAC TAC ATG AAC TGG GTC CGC 144  
 Ala Thr Ser Gly Phe Thr Phe Thr Asp Tyr Tyr Met Asn Trp Val Arg  
 25 30 35

CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG GGT TTT ATT AGA AAC AAA 192  
 Gln Pro Pro Gly Lys Ala Leu Glu Trp Léu Gly Phe Ile Arg Asn Lys  
 40 45 50

GCT AAT TAT TAC ACA ACA GAG TAC AGT GCA TGT GTG AAG GGT CGG TTC 240  
 Ala Asn Tyr Tyr Thr Thr Glu Tyr Ser Ala Ser Val Lys Gly Arg Phe  
 55 60 65 70

ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC CTC TAT CTT CAA ATG AAC 288  
Thr Ile Ser Arg Asp Asn Ser Gln Ser Ile Leu Gln Met Asn Thr Leu  
..... 75 ..... 80 ..... 85

ACC CTG AGA GCT GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA GAT GGG 336  
 Thr Leu Arg Ala Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg Asp Gly  
 90 95 100

TTC CTA CGG GAC TGG TAC TTC GAT GTC TGG GGC GCA GGG ACC ACG GTC 384  
 Phe Leu Arg Asp Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val  
 105 110 115

(2) INFORMATION FOR SEQ ID NO: 44:

- (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH: 354 base pairs  
(B) TYPE: nucleic acid  
(C) STRANDEDNESS: double  
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: mRNA  
(iii) HYPOTHETICAL: no  
(iv) ANTI-SENSE: no  
(v) ORIGINAL SOURCE:  
(A) ORGANISM: mouse

(ix) FEATURE:

(A) NAME/KEY:Clone 3KB11

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:

GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CCT CTG 48  
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Pro Leu  
5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100

GGG CAG AGG GCC ACC ATC TCA TAC AGG GCC AGC AAA AGT GTG CAG TTA 96  
 Gly Gln Arg Ala Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Gln Leu  
 20 25 30

CAT CTG GCT ATA GTT TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG I44  
 His Leu Ala Ile Val Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln  
 35 40 45

CCA CCC AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC ... 192  
 Pro Pro Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val Lys  
 50 55 60

CCT GCC AGG TTC AGT CGG AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC 240  
 Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn  
 65 70 75 80

ATC CAT CCT GTG GAG GAG GAT GCT GCA ACC ATAT ATAC ATGT TCA G CAC 1.288  
 Ile His Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His 5.  
                   85                  90                  95

ATT AGG GTA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA 1136  
 Ile Arg Val Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys 117  
       85 100                   85 105                   85 110

CGG GCT GAT GCT GCA CCA 345 TGT TGA CGC 351 AD E E YDD SVA LE 354  
 Arg Ala Asp Ala Ala Pro Tyr Ser Ile Val 352 DWD SIA GLS LLE 355  
 115 341 350 352

(2) INFORMATION FOR SEQ ID NO: 45: SEQ ID NO: 45 USE ST. 45 USE CAT 3 A 31 101

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 438 base pairs A

(B) TYPE:nucleic acid cat no. 1

(C) STANDEDNESS:double

**(D) TOPOLOGY: linear**

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL: no

(iv) ANTISENSE : no  
(v) ORIGINAL SOURCE : no

(vi) ORIGINAL SOURCE: 15A 112 760A 150 450 62

(A) ORGANISM:mouse

(ix) FEATURE: (A) NAME (KEY:Class 17KB1) BUREAU NUMBER:

(xi) (A) NAME/KEY:CLONE 1/RBT SEQUENCE DESCRIPTION: SEQ ID NO: 45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45

CTA TCG GTC CTC CTG CTC TGG GTT CCA CCT TCC AGT CCT GAC ATT CTC

CIA TGG GIA CIG CIG CIC TGG GII CCA CGG ICC ACT GGI GAC AII GIG  
Leu Trp Val Leu Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Ile Val

Red Trip Var Red Red Red Red Trip Var Red Red GUY Set Trip GUY Asp. Trip Var

10. *Chlorophytum comosum* (L.) Willd. (Asparagaceae) (Fig. 10)

2020-03-12 10:45:23.280 [main] INFO org.springframework.boot.SpringApplication - Starting application

CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG CAG AGG GCC 96  
 Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala  
 5 10 15

TCC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAT AGT 144  
 Ser Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser  
 20 25 30 35

TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG CCA CCC AGA CTC CTC 192  
 Tyr Met His Trp Asn Gln Gin Lys Pro Gly Gln Pro Pro Arg Leu Ieu  
 25 40 45 50

ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC CCT GCC AGG TTC AGT 240  
 Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val Pro Ala Arg Phe Ser  
 15 55 60 65

GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG 288  
 Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu  
 70 75 80

GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT AGG GGA GCT TAC 336  
 Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Arg Gly Ala Tyr  
 85 90 95

ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA CGG GCT GAT GCT GCA 394  
 Thr Phe Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala Ala  
 25 100 105 110 115

CCA ACT GTA TCC ATC TTC CCA CCA TCC AGT AAG CTT GGG AAA CGG TTC 432  
 Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Lys Leu Gly Lys Arg Phe  
 120 125 130

30 GCA CCG 438  
 Ala Pro

35 (2) INFORMATION FOR SEQ ID NO: 46:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 417 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:double
- (D) TOPOLOGY:linear

40 (ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

- (A) ORGANISM:mouse

45 (ix) FEATURE:

- (A) NAME/KEY:Clone 20KB1

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:46:

50 GGCCGCG GTGAGAACCG TTGGGAATTTC ATG GAG ACA GAC ACA CTC CTG 48  
 Met Glu Thr Asp Thr Leu Leu  
 -20 -15

CTA TGG GTA CTG CTG CTC TGG GTT CCA GGT TCC ACT GGT GAC ATT GTG 96  
 Leu Trp Val Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Ile Val  
 -10 -5 1  
 5

CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG CAG AGG GCC 144  
 Leu Thr Gln Ser Pro Ala Ser Leu Ala Val S r Leu Gly Gln Arg Ala  
 5 10 15

10 ACC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAT AGT 192  
 Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser  
 20 25 30

15 TAT ATG CAC TGG AAC CAA CAG AGA CCA GGA CAG CCA CCC AGA CTC CTC 240  
 Tyr Met His Trp Asn Gln Gln Arg Pro Gly Gln Pro Pro Arg Leu Leu  
 35 40 45

20 ATC TAT CTT GTA TCC AAC CTA GAC TCT GGG GTC CCT GCC AGG TTC AGT 288  
 Ile Tyr Leu Val Ser Asn Leu Asp Ser Gly Val Pro Ala Arg Phe Ser  
 50 55 60 65

25 GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG 336  
 Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu  
 70 75 80

30 GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT GAG GGA GCT TAC 384  
 Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Glu Gly Ala Tyr  
 85 90 95

ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA 417  
 Thr Phe Gly Gly Thr Lys Leu Glu Ile Lys  
 100 105

## (2) INFORMATION FOR SEQ ID NO: 47:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 420 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:single
- (D) TOPOLOGY:linear

## (ii) MOLECULE TYPE:mRNA

## (iii) HYPOTHETICAL:no

## (iv) ANTISENSE:no

## (vi) ORIGINAL SOURCE:

- (A) ORGANISM:mouse

## (ix) FEATURE:

- (A) NAME/KEY:Clone 27KA2

## (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 47:

GC GG CG CG CG TG AGA ACC GT TT GG GA AT TC AT C GAG ACA CAG TCC CAG 48  
 Met Glu Thr Gln Ser Gln  
 -20 -15

50 GTC TTT GTA TTC GTG TTT CTC TGG TTG TCT GGT GTT GAC GGA GAC ATT 96  
 Val Phe Val Phe Leu Trp Leu Ser Gly Val Asp Gly Asp Ile  
 -10 -5 1

GTG ATG ACC CAG TCT-CAC AAA TTC ATG TCC ACA TCA-GTA, GGA, GAC AGG 144  
 Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly Asp Arg  
 5 10 15

GTC AGT ATC ACC TGC AAG GCC AGT CAG GAT GTG AAT ACT GCT GTA GCC 192  
 Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala Val Ala  
 20 25 30

TGG TAT CAA CAG AAA CCA GGA CAA TCT CCT AAA CTA CTG CTT TAC TCG 240  
 Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Leu Tyr Ser  
 35 40 45 50

GCA TCC TAC CGG TAG ACT GGA GTC CCT GAT CAC TTC ACT GGC AGT GGA 288  
 Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp His Phe Thr Gly Ser Gly  
 55 60 65

TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC GGT GTG CAG GCT GAA GAC 336  
 Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Gly Val Gln Ala Glu Asp  
 70 75 80

CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT ACT CCT CCT CTC ACG TTC 384  
 Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Pro Pro Leu Thr Phe  
 85 90 95

GGT GCT GGG ACC AAG CTG GAA CTG AAA CGG GCT GAT 420  
 Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala Asp  
 100 105 110

(2) INFORMATION FOR SEQ ID NO: 48:

- (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH: 360 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: single  
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE:mRNA  
 (iii) HYPOTHETICAL: no  
 (iv) ANTISENSE: no  
 (vi) ORIGINAL SOURCE:  
 (A) ORGANISM:mouse  
 (ix) FEATURE:  
 (A) NAME/KEY:Clone 23KA26  
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:48

GGT GTT GAC GGA GAC ATT GTG ATG ACA CAG TCT CAC AAA TTC ATG TCC 48  
 Gly Val Asp Gly Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser  
 1 5 10

ACA TCA GTT GGA GAC AGG GTC ACC ATC ACC TGC AAG GCC AGT CAG GAT 96  
 Thr Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp  
 15 20 25

GTG ACT ACT GAT GTA GCC TGG TAT CAA CAG AAA CCA CGA CAA TCT CCT 144  
 Val Thr Thr Asp Val Ala Trp Tyr Gln Gln Lys Pro Arg Gln Ser Pro  
 30 35 40

AAA CTA CTG ATT TAC TCG GCA TCC TAT CGG TAC ACT GGA GTC CCT GAT 192  
 Lys Leu Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp 192  
 5 45 50 55

CGC TTC ACT GGC AGT GGA TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC 240  
 Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Ph Thr Phe Thr Ile Ser 240  
 10 60 65 70 75

AGT GTG CAG GCT GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT 286  
 Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr 286  
 15 80 85 90

AGT ACT GCG TGG ACG TTC GGT GGC ACC AAG CTG GAA ATC AAA CCG 336  
 Ser Thr Ala Trp Thr Phe GLY Gly Thr Lys Leu Glu Ile Lys Arg 336  
 15 95 100 105

GCT GAT GCT GCA CGA ACT GTA TCG 360  
 Ala Asp Ala Ala Pro Thr Val Ser 360  
 20 110 115

25 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100 105 110 115 120 125 130 135 140 145 150 155 160 165 170 175 180 185 190 195 200 205 210 215 220 225 230 235 240 245 250 255 260 265 270 275 280 285 290 295 300 305 310 315 320 325 330 335 340 345 350 355 360 365 370 375 380 385 390 395 400 405 410 415 420 425 430 435 440 445 450 455 460 465 470 475 480 485 490 495 500 505 510 515 520 525 530 535 540 545 550 555 560 565 570 575 580 585 590 595 600 605 610 615 620 625 630 635 640 645 650 655 660 665 670 675 680 685 690 695 700 705 710 715 720 725 730 735 740 745 750 755 760 765 770 775 780 785 790 795 800 805 810 815 820 825 830 835 840 845 850 855 860 865 870 875 880 885 890 895 900 905 910 915 920 925 930 935 940 945 950 955 960 965 970 975 980 985 990 995 1000 1005 1010 1015 1020 1025 1030 1035 1040 1045 1050 1055 1060 1065 1070 1075 1080 1085 1090 1095 1100 1105 1110 1115 1120 1125 1130 1135 1140 1145 1150 1155 1160 1165 1170 1175 1180 1185 1190 1195 1200 1205 1210 1215 1220 1225 1230 1235 1240 1245 1250 1255 1260 1265 1270 1275 1280 1285 1290 1295 1300 1305 1310 1315 1320 1325 1330 1335 1340 1345 1350 1355 1360 1365 1370 1375 1380 1385 1390 1395 1400 1405 1410 1415 1420 1425 1430 1435 1440 1445 1450 1455 1460 1465 1470 1475 1480 1485 1490 1495 1500 1505 1510 1515 1520 1525 1530 1535 1540 1545 1550 1555 1560 1565 1570 1575 1580 1585 1590 1595 1600 1605 1610 1615 1620 1625 1630 1635 1640 1645 1650 1655 1660 1665 1670 1675 1680 1685 1690 1695 1700 1705 1710 1715 1720 1725 1730 1735 1740 1745 1750 1755 1760 1765 1770 1775 1780 1785 1790 1795 1800 1805 1810 1815 1820 1825 1830 1835 1840 1845 1850 1855 1860 1865 1870 1875 1880 1885 1890 1895 1900 1905 1910 1915 1920 1925 1930 1935 1940 1945 1950 1955 1960 1965 1970 1975 1980 1985 1990 1995 2000 2005 2010 2015 2020 2025 2030 2035 2040 2045 2050 2055 2060 2065 2070 2075 2080 2085 2090 2095 2100 2105 2110 2115 2120 2125 2130 2135 2140 2145 2150 2155 2160 2165 2170 2175 2180 2185 2190 2195 2200 2205 2210 2215 2220 2225 2230 2235 2240 2245 2250 2255 2260 2265 2270 2275 2280 2285 2290 2295 2300 2305 2310 2315 2320 2325 2330 2335 2340 2345 2350 2355 2360 2365 2370 2375 2380 2385 2390 2395 2400 2405 2410 2415 2420 2425 2430 2435 2440 2445 2450 2455 2460 2465 2470 2475 2480 2485 2490 2495 2500 2505 2510 2515 2520 2525 2530 2535 2540 2545 2550 2555 2560 2565 2570 2575 2580 2585 2590 2595 2600 2605 2610 2615 2620 2625 2630 2635 2640 2645 2650 2655 2660 2665 2670 2675 2680 2685 2690 2695 2700 2705 2710 2715 2720 2725 2730 2735 2740 2745 2750 2755 2760 2765 2770 2775 2780 2785 2790 2795 2800 2805 2810 2815 2820 2825 2830 2835 2840 2845 2850 2855 2860 2865 2870 2875 2880 2885 2890 2895 2900 2905 2910 2915 2920 2925 2930 2935 2940 2945 2950 2955 2960 2965 2970 2975 2980 2985 2990 2995 3000 3005 3010 3015 3020 3025 3030 3035 3040 3045 3050 3055 3060 3065 3070 3075 3080 3085 3090 3095 3100 3105 3110 3115 3120 3125 3130 3135 3140 3145 3150 3155 3160 3165 3170 3175 3180 3185 3190 3195 3200 3205 3210 3215 3220 3225 3230 3235 3240 3245 3250 3255 3260 3265 3270 3275 3280 3285 3290 3295 3300 3305 3310 3315 3320 3325 3330 3335 3340 3345 3350 3355 3360 3365 3370 3375 3380 3385 3390 3395 3400 3405 3410 3415 3420 3425 3430 3435 3440 3445 3450 3455 3460 3465 3470 3475 3480 3485 3490 3495 3500 3505 3510 3515 3520 3525 3530 3535 3540 3545 3550 3555 3560 3565 3570 3575 3580 3585 3590 3595 3600 3605 3610 3615 3620 3625 3630 3635 3640 3645 3650 3655 3660 3665 3670 3675 3680 3685 3690 3695 3700 3705 3710 3715 3720 3725 3730 3735 3740 3745 3750 3755 3760 3765 3770 3775 3780 3785 3790 3795 3800 3805 3810 3815 3820 3825 3830 3835 3840 3845 3850 3855 3860 3865 3870 3875 3880 3885 3890 3895 3900 3905 3910 3915 3920 3925 3930 3935 3940 3945 3950 3955 3960 3965 3970 3975 3980 3985 3990 3995 4000 4005 4010 4015 4020 4025 4030 4035 4040 4045 4050 4055 4060 4065 4070 4075 4080 4085 4090 4095 4100 4105 4110 4115 4120 4125 4130 4135 4140 4145 4150 4155 4160 4165 4170 4175 4180 4185 4190 4195 4200 4205 4210 4215 4220 4225 4230 4235 4240 4245 4250 4255 4260 4265 4270 4275 4280 4285 4290 4295 4300 4305 4310 4315 4320 4325 4330 4335 4340 4345 4350 4355 4360 4365 4370 4375 4380 4385 4390 4395 4400 4405 4410 4415 4420 4425 4430 4435 4440 4445 4450 4455 4460 4465 4470 4475 4480 4485 4490 4495 4500 4505 4510 4515 4520 4525 4530 4535 4540 4545 4550 4555 4560 4565 4570 4575 4580 4585 4590 4595 4600 4605 4610 4615 4620 4625 4630 4635 4640 4645 4650 4655 4660 4665 4670 4675 4680 4685 4690 4695 4700 4705 4710 4715 4720 4725 4730 4735 4740 4745 4750 4755 4760 4765 4770 4775 4780 4785 4790 4795 4800 4805 4810 4815 4820 4825 4830 4835 4840 4845 4850 4855 4860 4865 4870 4875 4880 4885 4890 4895 4900 4905 4910 4915 4920 4925 4930 4935 4940 4945 4950 4955 4960 4965 4970 4975 4980 4985 4990 4995 5000 5005 5010 5015 5020 5025 5030 5035 5040 5045 5050 5055 5060 5065 5070 5075 5080 5085 5090 5095 5100 5105 5110 5115 5120 5125 5130 5135 5140 5145 5150 5155 5160 5165 5170 5175 5180 5185 5190 5195 5200 5205 5210 5215 5220 5225 5230 5235 5240 5245 5250 5255 5260 5265 5270 5275 5280 5285 5290 5295 5300 5305 5310 5315 5320 5325 5330 5335 5340 5345 5350 5355 5360 5365 5370 5375 5380 5385 5390 5395 5400 5405 5410 5415 5420 5425 5430 5435 5440 5445 5450 5455 5460 5465 5470 5475 5480 5485 5490 5495 5500 5505 5510 5515 5520 5525 5530 5535 5540 5545 5550 5555 5560 5565 5570 5575 5580 5585 5590 5595 5600 5605 5610 5615 5620 5625 5630 5635 5640 5645 5650 5655 5660 5665 5670 5675 5680 5685 5690 5695 5700 5705 5710 5715 5720 5725 5730 5735 5740 5745 5750 5755 5760 5765 5770 5775 5780 5785 5790 5795 5800 5805 5810 5815 5820 5825 5830 5835 5840 5845 5850 5855 5860 5865 5870 5875 5880 5885 5890 5895 5900 5905 5910 5915 5920 5925 5930 5935 5940 5945 5950 5955 5960 5965 5970 5975 5980 5985 5990 5995 6000 6005 6010 6015 6020 6025 6030 6035 6040 6045 6050 6055 6060 6065 6070 6075 6080 6085 6090 6095 6100 6105 6110 6115 6120 6125 6130 6135 6140 6145 6150 6155 6160 6165 6170 6175 6180 6185 6190 6195 6200 6205 6210 6215 6220 6225 6230 6235 6240 6245 6250 6255 6260 6265 6270 6275 6280 6285 6290 6295 6300 6305 6310 6315 6320 6325 6330 6335 6340 6345 6350 6355 6360 6365 6370 6375 6380 6385 6390 6395 6400 6405 6410 6415 6420 6425 6430 6435 6440 6445 6450 6455 6460 6465 6470 6475 6480 6485 6490 6495 6500 6505 6510 6515 6520 6525 6530 6535 6540 6545 6550 6555 6560 6565 6570 6575 6580 6585 6590 6595 6600 6605 6610 6615 6620 6625 6630 6635 6640 6645 6650 6655 6660 6665 6670 6675 6680 6685 6690 6695 6700 6705 6710 6715 6720 6725 6730 6735 6740 6745 6750 6755 6760 6765 6770 6775 6780 6785 6790 6795 6800 6805 6810 6815 6820 6825 6830 6835 6840 6845 6850 6855 6860 6865 6870 6875 6880 6885 6890 6895 6900 6905 6910 6915 6920 6925 6930 6935 6940 6945 6950 6955 6960 6965 6970 6975 6980 6985 6990 6995 7000 7005 7010 7015 7020 7025 7030 7035 7040 7045 7050 7055 7060 7065 7070 7075 7080 7085 7090 7095 7100 7105 7110 7115 7120 7125 7130 7135 7140 7145 7150 7155 7160 7165 7170 7175 7180 7185 7190 7195 7200 7205 7210 7215 7220 7225 7230 7235 7240 7245 7250 7255 7260 7265 7270 7275 7280 7285 7290 7295 7300 7305 7310 7315 7320 7325 7330 7335 7340 7345 7350 7355 7360 7365 7370 7375 7380 7385 7390 7395 7400 7405 7410 7415 7420 7425 7430 7435 7440 7445 7450 7455 7460 7465 7470 7475 7480 7485 7490 7495 7500 7505 7510 7515 7520 7525 7530 7535 7540 7545 7550 7555 7560 7565 7570 7575 7580 7585 7590 7595 7600 7605 7610 7615 7620 7625 7630 7635 7640 7645 7650 7655 7660 7665 7670 7675 7680 7685 7690 7695 7700 7705 7710 7715 7720 7725 7730 7735 7740 7745 7750 7755 7760 7765 7770 7775 7780 7785 7790 7795 7800 7805 7810 7815 7820 7825 7830 7835 7840 7845 7850 7855 7860 7865 7870 7875 7880 7885 7890 7895 7900 7905 7910 7915 7920 7925 7930 7935 7940 7945 7950 7955 7960 7965 7970 7975 7980 7985 7990 7995 8000 8005 8010 8015 8020 8025 8030 8035 8040 8045 8050 8055 8060 8065 8070 8075 8080 8085 8090 8095 8100 8105 8110 8115 8120 8125 8130 8135 8140 8145 8150 8155 8160 8165 8170 8175 8180 8185 8190 8195 8200 8205 8210 8215 8220 8225 8230 8235 8240 8245 8250 8255 8260 8265 8270 8275 8280 8285 8290 8295 8300 8305 8310 8315 8320 8325 8330 8335 8340 8345 8350 8355 8360 8365 8370 8375 8380 8385 8390 8395 8400 8405 8410 8415 8420 8425 8430 8435 8440 8445 8450 8455 8460 8465 8470 8475 8480 8485 8490 8495 8500 8505 8510 8515 8520 8525 8530 8535 8540 8545 8550 8555 8560 8565 8570 8575 8580 8585 8590 8595 8600 8605 8610 8615 8620 8625 8630 8635 8640 8645 8650 8655 8660 8665 8670 8675 8680 8685 8690 8695 8700 8705 8710 8715 8720 8725 8730 8735 8740 8745 8750 8755 8760 8765 8770 8775 8780 8785 8790 8795 8800 8805 8810 8815 8820 8825 8830 8835 8840 8845 8850 8855 8860 8865 8870 8875 8880 8885 8890 8895 8900 8905 8910 8915 8920 8925 8930 8935 8940 8945 8950 8955 8960 8965 8970 8975 8980 8985 8990 8995 9000 9005 9010 9015 9020 9025 9030 9035 9040 9045 9050 9055 9060 9065 9070 9075 9080 9085 9090 9095 9100 9105 9110 9115 9120 9125 9130 9135 9140 9145 9150 9155 9160 9165 9170 9175 9180 9185 9190 9195 9200 9205 9210 9215 9220 9225 9230 9235 9240 9245 9250 9255 9260 9265 9270 9275 9280 9285 9290 9295 9300 9305 9310 9315 9320 9325 9330 9335 9340 9345 9350 9355 9360 9365 9370 9375 9380 9385 9390 9395 9400 9405 9410 9415 9420 9425 9430 9435 9440 9445 9450 9455 9460 9465 9470 9475 9480 9485 9490 9495 9500 9505 9510 9515 9520 9525 9530 9535 9540 9545 9550 9555 9560 9565 9570 9575 9580 9585 9590 9595 9600 9605 9610 9615 9620 9625 9630 9635 9640 9645 9650 9655 9660 9665 9670 9675 9680 9685 9690 9695 9700 9705 9710 9715 9720 9725 9730 9735 9740 9745 9750 9755 9760 9765 9770 9775 9780 9785 9790 9795 9800 9805 9810 9815 9820 9825 9830 9835 9840 9845 9850 9855 9860 9865 9870 9875 9880 9885 9890 9895 9900 9905 9910 9915 9920 9925 9930 9935 9940 9945 9950 9955 9960 9965 9970 9975 9980 9985 9990 9995 9999

25 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100 105 110 115 120 125 130 135 140 145 150 155 160 165 170 175 180 185 190 195 200 205 210 215 220 225 230 235 240 245 250 255 260 265 270 275 280 285 290 295 300 305 310 315 320 325 330 335 340 345 350 355 360 365 370 375 380 385 390 395 400 405 410 415 420 425 430 435 440 445 450 455 460 465 470 475 480 485 490 495 500 505 510 515 520 525 530 535 540 545 550 555 560 565 570 575 580 585 590 595 600 605 610 615 620 625 630 635 640 645 650 655 660 665 670 675 680 685 690 695 700 705 710 715 720 725 730 735 740 745 750 755 760 765 770 775 780 785 790 795 800 805 810 815 820 825 830 835 840 845 850 855 860 865 870 875 880 885 890 895 900 905 910 915 920 925 930 935 940 945 950 955 960 965 970 975 980 985 990 995 1000 1005 1010 1015 1020 1025 1030 1035 1040 1045 1050 1055 1060 1065 1070 1075 1080 1085 1090 1095 1100 1105 1110 1115 1120 1125 1130 1135 1140 1145 1150 1155 1160 1165 1170 1175 1180 1185 1190 1195 1200 1205 1210 1215

and a hypervariable region CDR<sub>3</sub> having an amino acid sequence selected from

(3) Glu Glu Tyr Asp Tyr Asp  
 5 Thr Leu Asp Tyr;  
 Asp Arg Gly Gly Arg Asp  
 Trp Tyr Phe Asp Val;  
 10 Asp Gly Phe Leu Arg Asp  
 Trp Tyr Phe Asp Val; and  
 Ser Gly Tyr Tyr Gly Ser  
 Phe Val Gly Phe Ala Tyr .

15

2. An immunoglobulin H chain variable region fragment having the following amino acid sequence

20

Glu Val Gln Leu Gln Gln Ser Gly Thr Val  
 Leu Ala Arg Pro Gly Ala Ser Val Lys Met  
 Ser Cys Lys Ala Ser Gly Tyr Thr Phe Asn  
 Ser Tyr Trp Met His Trp Val Lys Gln Arg  
 25 Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala  
 Ile Tyr Pro Gly Asn Ser Asp Ile Ser Tyr  
 Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu  
 Thr Ala Val Thr Ser Thr Ser Ala Tyr  
 Met Glu Leu Arg Ser Leu Thr Asn Glu Asp  
 Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu  
 30 Tyr Asp Tyr Asp Thr Leu Asp Tyr Trp Gly  
 Gin Gly Thr Ser Val Thr Val Ser Ser

35

40

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55

## 3. An immunoglobulin H chain variable region fragment having the following amino acid sequence

5           Glu Val Lys Leu Val Glu Ser Gly Gly Gly  
 Leu Val Gln Pro Gly Gly Ser Leu Arg Leu  
 Ser Cys Ala Thr Ser Gly Phe Thr Phe Thr  
 Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro  
 Pro Gly Lys Ala Leu Glu Trp Leu Gly Phe  
 Ile Arg Asn Lys Ala Asn Tyr Tyr Thr Thr  
 Glu Tyr Ser Ala Ser Val Lys Gly Arg Phe  
 Thr Ile Ser Arg Asp Asn Ser Gln Ser Ile  
 10          Leu Tyr Leu Gln Met Asn Thr Leu Arg Ala  
 Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg  
 Asp Gly Phe Leu Arg Asp Trp Tyr Phe Asp  
 Val Trp Gly Ala Gly Thr Thr Val Thr Val  
 15          Ser Ser.  
 20  
 25  
 30  
 35  
 40  
 45

## 25 4. An immunoglobulin H chain variable region fragment having the following amino acid sequence

30          Glu Val Lys Leu Val Glu Ser Gly Gly Gly  
 Leu Val Gln Pro Gly Gly Ser Leu Arg Leu  
 Ser Cys Ala Thr Ser Gly Leu Thr Phe Thr  
 Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro  
 Pro Gly Lys Glu Leu Glu Trp Leu Gly Phe  
 Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr  
 Asp Tyr Ser Ala Ser Val Lys Gly Arg Phe  
 Thr Ile Ser Arg Asp Asn Pro Gln Ser Ile  
 Leu Tyr Leu Gln Met Asn Thr Leu Thr Thr  
 Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg  
 Asp Arg Gly Gly Arg Asp Trp Tyr Phe Asp  
 Val Trp Gly Ala Gly Thr Thr Val Thr Val  
 Ser Ser.  
 45

## 5. An immunoglobulin H chain variable region fragment having the following amino acid sequence

5           Glu Val Gln Leu Gln Gln Ser Gly Ala Glu  
 10          Leu Ala Arg Pro Gly Ala Ser Val Asn Leu  
 15          Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr  
 20          Asn Tyr Trp Met Gln Trp Val Lys Gln Arg  
 25          Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala  
 30          Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr  
 35          Thr Gln Lys Phe Lys Gly Lys Ala Thr Leu  
 40          Thr Ala Ala Lys Ser Ser Ser Thr Ala Tyr  
 45          Met Gln Leu Ser Ser Leu Ala Ser Glu Asp  
 50          Ser Ala Val Tyr Tyr Cys Ala Arg Ser Gly  
 55          Tyr Tyr Gly Ser Phe Val Gly Phe Ala Tyr  
 60          Trp Gly Gln Gly Thr Leu Val Thr Val Ser  
 65          Ala .

## 25 6. DNA and RNA fragments each encoding an immunoglobulin H chain variable region fragment which contains a base sequence encoding a hypervariable region CDR1 having an amino acid sequence selected from

30          (1) Ser Tyr Trp Met His;  
 35          (2) Asp Tyr Tyr Met Asn; and  
 40          (3) Asn Tyr Trp Met Gln;

a base sequence encoding a hypervariable region CDR2 having an amino acid sequence selected from

45          (1) Ala Ile Tyr Pro Gly Asn Ser  
 50          Asp Ile Ser Tyr Ser Gln Asn  
 55          Phe Lys Asp;  
 60          Phe Ile Arg Asn Lys Ala  
 65          Asn Leu Tyr Thr Thr Asp  
 70          Tyr Ser Ala Ser Val Lys  
 75          Gly;  
 80          Phe Ile Arg Asn Lys Ala  
 85          Asn Tyr Tyr Thr Thr Glu  
 90          Tyr Ser Ala Ser Val Lys  
 95          Gly; and  
 100         Ala Ile Tyr Pro Gly Asp  
 105         Gly Asp Thr Arg Tyr Thr  
 110         Glu Lys Phe Lys Gly ,

a base sequence encoding a hypervariable region CDR3 having an amino acid sequence selected from

(3) Glu Glu Tyr Asp Tyr Asp

5 Thr Leu Asp Tyr;  
 Asp Arg Gly Gly Arg Asp  
 Trp Tyr Phe Asp Val;  
 10 Asp Gly Phe Leu Arg Asp  
 Trp Tyr Phe Asp Val; and  
 Ser Gly Tyr Tyr Gly Ser  
 Phe Val Gly Phe Ala Tyr

15 Asp Gly Phe Leu Arg Asp  
 Trp Tyr Phe Asp Val; and  
 Ser Gly Tyr Tyr Gly Ser  
 Phe Val Gly Phe Ala Tyr

7. An immunoglobulin H chain variable region fragment having following base sequence:

20 GAG GTT CAG CTC CAG CAG TCT GGG ACT GTG  
 CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG  
 TCC TGC AAG GCT TCG GGC TAC ACC TTT AAC  
 25 AGC TAC TGG ATG CAC TGG GTA AAA CAG AGG  
 CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG  
 ATT TAT CCT GGA AAT AGT GAT ATT AGC TAC  
 30 AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG  
 ACT GCC GTC ACA TCC ACC AGC ACT GCC TAC  
 ATG GAA CTC AGA AGC CTG ACA AAT GAG GAC  
 TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA  
 35 TAT GAT TAC GAC ACC CTG GAC TAC TGG GGT  
 CAA GGA ACC TCA GTC ACC GTC TCC TCA.

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## 8. An immunoglobulin H chain variable region fragment having the following base sequence.

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GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC  
 TTG GTA CAG CCT GGG GGT TCT CTC AGA CTC  
 TCC TGT GCA ACT TCT GGG TTA ACC TTC ACT  
 GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT  
 CCA GGA AAG GAA CTT GAA TGG TTG GGT TTT  
 ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA  
 GAC TAC AGT GCA TCT GTG AAG GGT CGG TTC  
 ACC ATC TCC AGA GAT AAT CCC CAA AGC ATC  
 CTC TAT CTT CAA ATG AAC ACC CTG ACA ACT  
 GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA  
 GAT AGG GGG GGG AGG GAC TGG TAC TTC GAT  
 GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC  
 TCC TCA .

## 9. An immunoglobulin H chain variable region fragment having the following base sequence

GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC  
 TTG GTA CAG CCT GGG GGT TCT CTG AGA CTC  
 TCC TGT GCA ACT TCT GGG TTC ACC TTC ACT  
 GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT  
 CCA GGA AAG GCA CTT GAG TGG TTG GGT TTT  
 ATT AGA AAC AAA GCT AAT TAT TAC ACA ACA  
 GAG TAC AGT GCA TCT GTG AAG GGT CGG TTC  
 ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC  
 CTC TAT CTT CAA ATG AAC ACC CTG AGA GCT  
 GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA  
 GAT GGG TTC CTA CGG GAC TGG TAC TTC GAT  
 GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC  
 TCC TCA .

10. An immunoglobulin H chain variable region fragment having the following base sequence

GAG GTT CAG CTC CAG CAG TCT GGG GCT GAA  
CTG GCA AGA CCT GGG GCT TCA GTG AAC TTG  
TCC TGC AAG GCT TCT GGC TAC ACC TTT ACT  
AAC TAC TGG ATG CAG TGG GTA AAA CAG AGG  
CCT GGA CAG GGT CTG GAA TGG ATT GGG GCT  
ATT TAT CCT GGA GAT GGT GAT ACT AGG TAC  
ACT CAG AAG TTC AAG GGC AAG GCC ACA TTG  
ACT GCA GCT AAA TCC TCC AGC ACA GCC TAC  
ATG CAA CTC AGC AGC TTG GCA TCT GAG GAC  
TCT GCG GTC TAT TAC TGT GCA AGA TCG GGC  
TAC TAT GGT AGC TTC GTT GGG TTT GCT TAC  
TGG GGC CAA GGG ACT CTG GTC ACT GTC TCT  
GCA .

- 25 11. An immunoglobulin L chain variable region fragment which contains a hypervariable region CDR1 having an amino acid sequence selected from

(1) Tyr Arg Ala Ser Lys Ser Val  
 Gin Leu His Leu Ala Ile Val  
 Tyr Met His  
 Tyr Arg Ala Ser Lys Ser Val  
 Ser Thr Ser Gly Tyr Ser Tyr  
 Met His  
 Lys Ala Ser Gln Asp Val Asn  
 Thr Ala Val Ala  
 Lys Ala Ser Gln Asp Val Thr  
 Thr Asp Val Ala  
 Thr Asp Val Ala

a hypervariable region CDR2 having an amino acid sequence selected from

(2) Leu Val Ser Asn Leu Glu Ser;  
 Leu Val Ser Asn Leu Asp Ser; and  
 Ser Ala Ser Tyr Arg Tyr Thr,

and a hypervariable region CDR3 having an amino acid sequence selected from:

- (3) Gln His Ile Arg Val Ala Tyr  
 5 Thr;  
 Gln His Ile Arg Gly Ala Tyr  
 10 Thr;  
 Gln His Ile Glu Gly Ala Tyr  
 15 Thr;  
 Gln Gln His Tyr Ser Pro Pro  
 Leu Thr; and  
 Gln Gln His Tyr Ser Thr Ala  
 Trp Thr.

20 12. An immunoglobulin L chain variable region fragment having the following amino acid sequence

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser  
 25 Leu Ala Val Ser Pro Leu Gly Gln Arg Ala  
 Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val  
 Gln Leu His Leu Ala Ile Val Tyr Met His  
 Trp Asn Gln Gln Lys Pro Gly Gln Pro Pro  
 30 Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu  
 Glu Ser Gly Val Pro Ala Arg Phe Ser Gly  
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn  
 Ile His Pro Val Glu Glu Asp Ala Ala  
 Thr Tyr Tyr Cys Gln His Ile Arg Val Ala  
 Tyr Thr Phe Gly Gly Thr Lys Leu Glu  
 35 Ile Lys.

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## 13. An immunoglobulin L chain variable region fragment having the following amino acid sequence

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Asp Ile Val Leu Thr Gln Ser Pro Ala Ser  
 Leu Ala Val Ser Leu Gly Gln Arg Ala Ser  
 Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser  
 Thr Ser Gly Tyr Ser Tyr Met His Trp Asn  
 Gln Gln Lys Pro Gly Gln Pro Pro Arg Leu  
 Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser  
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly  
 Ser Gly Thr Asp Phe Thr Leu Asn Ile His  
 Pro Val Glu Glu Asp Ala Ala Thr Tyr  
 Tyr Cys Gln His Ile Arg Gly Ala Tyr Thr  
 Phe Gly Gly Thr Lys Leu Glu Ile Lys.

## 14. An immunoglobulin L chain variable region fragment having the following amino acid sequence

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Asp Ile Val Leu Thr Gln Ser Pro Ala Ser  
 Leu Ala Val Ser Leu Gly Gln Arg Ala Thr  
 Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser  
 Thr Ser Gly Tyr Ser Tyr Met His Trp Asn  
 Gln Gln Arg Pro Gly Gln Pro Pro Arg Leu  
 Leu Ile Tyr Leu Val Ser Asn Leu Asp Ser  
 Gly Val Pro Ala Arg Phe Ser Gly Ser Gly  
 Ser Gly Thr Asp Phe Thr Leu Asn Ile His  
 Pro Val Glu Glu Asp Ala Ala Thr Tyr  
 Tyr Cys Gln His Ile Glu Gly Ala Tyr Thr  
 Phe Gly Gly Thr Lys Leu Glu Ile Lys.

## 15. An immunoglobulin L chain variable region fragment having the following amino acid sequence

Asp Ile Val Met Thr Gln Ser His Lys Phe  
 5 Met Ser Thr Ser Val Gly Asp Arg Val Ser  
 Ile Thr Cys Lys Ala Ser Gln Asp Val Asn  
 Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro  
 10 Gly Gln Ser Pro Lys Leu Leu Leu Tyr Ser  
 Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp  
 His Phe Thr Gly Ser Gly Ser Gly Thr Asp  
 Phe Thr Phe Thr Ile Ser Gly Val Gln Ala  
 15 Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln  
 His Tyr Ser Pro Pro Leu Thr Phe Gly Ala  
 Gly Thr Lys Leu Glu Leu Lys .

## 16. An immunoglobulin L chain variable region fragment having the following amino acid sequence

20 Asp Ile Val Met Thr Gln Ser His Lys Phe  
 Met Ser Thr Ser Val Gly Asp Arg Val Thr  
 Ile Thr Cys Lys Ala Ser Gln Asp Val Thr  
 25 Thr Asp Val Ala Trp Tyr Gln Gln Lys Pro  
 Arg Gln Ser Pro Lys Leu Leu Ile Tyr Ser  
 Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp  
 Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp  
 Phe Thr Phe Thr Ile Ser Ser Val Gln Ala  
 30 Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln  
 His Tyr Ser Thr Ala Trp Thr Phe Gly Gly  
 35 Gly Thr Lys Leu Glu Ile Lys .

17. DNA and RNA fragments each encoding an immunoglobulin L-chain variable region fragment which contains a base sequence encoding a hypervariable region CDR1 having an amino acid sequence selected from

- (1) Tyr Arg Ala Ser Lys Ser Val  
Gln Leu His Leu Ala Ile Val  
Tyr Met His;  
Tyr Arg Ala Ser Lys Ser Val  
Ser Thr Ser Gly Tyr Ser Tyr  
Met His;  
Lys Ala Ser Gln Asp Val Asn  
Thr Ala Val Ala; and  
Lys Ala Ser Gln Asp Val Thr  
Thr Asp Val Ala.

**20 a base sequence encoding a hypervariable region CDR2 having an amino acid sequence selected from**

- (2) Leu Val Ser Asn Leu Glu Ser;  
Leu Val Ser Asn Leu Asp Ser; and  
Ser Ala Ser Tyr Arg Tyr Thr.

and a base sequence encoding a hypervariable region CDR3 having an amino acid sequence selected from

- (3) Gln His Ile Arg Val Ala Tyr  
 Thr;  
 Gln His Ile Arg Gly Ala Tyr  
 Thr;  
 Gln His Ile Glu Gly Ala Tyr  
 Thr;  
 Gln Gln His Tyr Ser Pro Pro.  
 Leu Thr; and  
 Gln Gln His Tyr Ser Thr Ala  
 Trp Thr.

## 18. An immunoglobulin L chain variable region fragment having the following base sequence

GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC  
 5 TTA GCT GTA TCT CCT CTG GGG CAG AGG GCC  
 ACC ATC TCA TAC AGG GCC AGC AAA AGT GTG  
 CAG TTA CAT CTG GCT ATA GTT TAT ATG CAC  
 10 TGG AAC CAA CAG AAA CCA GGA CAG CCA CCC  
 AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA  
 GAA TCT GGG GTC CCT GCC AGG TTC AGT GGC  
 AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC  
 15 ATC CAT CCT GTG GAG GAG GAG GAT GCT GCA  
 ACC TAT TAC TGT CAG CAC ATT AGG GTA GCT  
 TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA  
 ATA AAA .

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## 19. An immunoglobulin L chain variable region fragment having the following base sequence

25 GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC  
 TTA GCT GTA TCT CTG GGG CAG AGG GCC TCC  
 ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT  
 ACA TCT GGC TAT AGT TAT ATG CAC TGG AAC  
 30 CAA CAG AAA CCA GGA CAG CCA CCC AGA CTC  
 CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT  
 GGG GTC CCT GCC AGG TTC AGT GGC AGT GGG  
 35 TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT  
 CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT  
 TAC TGT CAG CAC ATT AGG GGA GCT TAC ACG  
 40 TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA .

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## 20. An immunoglobulin L chain variable region fragment having the following base sequence

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GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC
TTA GCT GTA TCT CTG GGG CAG AGG GCC ACC
ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT
ACA TCT GGC TAT AGT TAT ATG CAC TGG AAC
CAA CAG AGA CCA GGA CAG CCA CCC AGA CTC
CTC ATC TAT CTT GTA TCC AAC CTA GAC TCT
GGG GTC CCT GCC AGG TTC AGT GGC AGT GGG
TGT GGG ACA GAC TTC ACC CTC AAC ATC CAT
CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT
TAC ATGT CAG CAC ATT GAG GGA GCT TAC ACG
TTC GGA GGG ACC AAG CTG GAA ATA AAA .

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21. A D6

## 21. An immunoglobulin L chain variable region fragment having the following base sequence

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GAC ATT GTG ATG ACC CAG TCT CAC AAA TTC
ATG TCC ACA TCA GTA GGA GAC AGG GTC AGT
ATC ACC TGC AAG GCC AGT CAG GAT GTG AAT
ACT GCT GTA GCC TGG TAT CAA CAG AAA CCA
GGA CAA TCT CCT AAA CTA CTG CTT TAC TCG
GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT
CAC TTC ACT GGC AGT GGA TCT GGG ACG GAT
TTC ACT TTC ACC ATC AGC GGT GTG CAG GCT
GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA
CAT TAT AGT CCT CCT CTC ACG TTC GGT GCT
GGG ACC AAG CTG GAA CTG AAA .

```

## 22. An immunoglobulin L chain variable region fragment having the following base sequence

GAC ATT GTG ATG ACA CAG TCT CAC AAA TTC  
5 ATG TCC ACA TCA GTT GGA GAC AGG GTC ACC  
ATC ACC TGC AAG GCC AGT CAG GAT GTG ACT  
ACT GAT GTA GCC TGG TAT CAA CAG AAA CCA  
CGA CAA TCT CCT AAA CTA CTG ATT TAC TCG  
10 GCA TCC TAT CGG TAC ACT GGA GTC CCT GAT  
CGC TTC ACT GGC AGT GGA TCT GGG ACG GAT  
TTC ACT TTC ACC ATC AGC AGT GTG CAG GCT  
GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA  
CAT TAT AGT ACT GCG TGG ACG TTC GGT GGT  
15 GGC ACC AAG CTG GAA ATC AAA .

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## 23. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 2 and the immunoglobulin L chain variable region fragment according to claim 12.

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## 24. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 2 and the immunoglobulin L chain variable region fragment according to claim 13.

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## 25. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 3 and the immunoglobulin L chain variable region fragment according to claim 14.

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## 26. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 4 and the immunoglobulin L chain variable region fragment according to claim 15.

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ON BEHALF OF THE UNIVERSITY OF TORONTO LIBRARIES

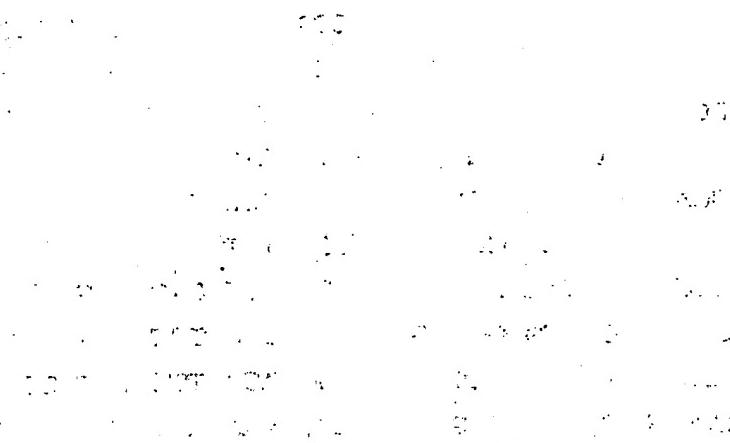


FIG. I

**Idio 3**

	$\lambda$	K	G3	G2b	G2a	G1	M	A
+		X	G3	G2b	G2a	G1	M	A
+		X	G3	G2b	G2a	G1	M	A
+		X	G3	G2b	G2a	G1	M	A
+		X	G3	G2b	G2a	G1	M	A

**Idio 17****Idio 20****Idio 27****Idio 33**

FIG. 2

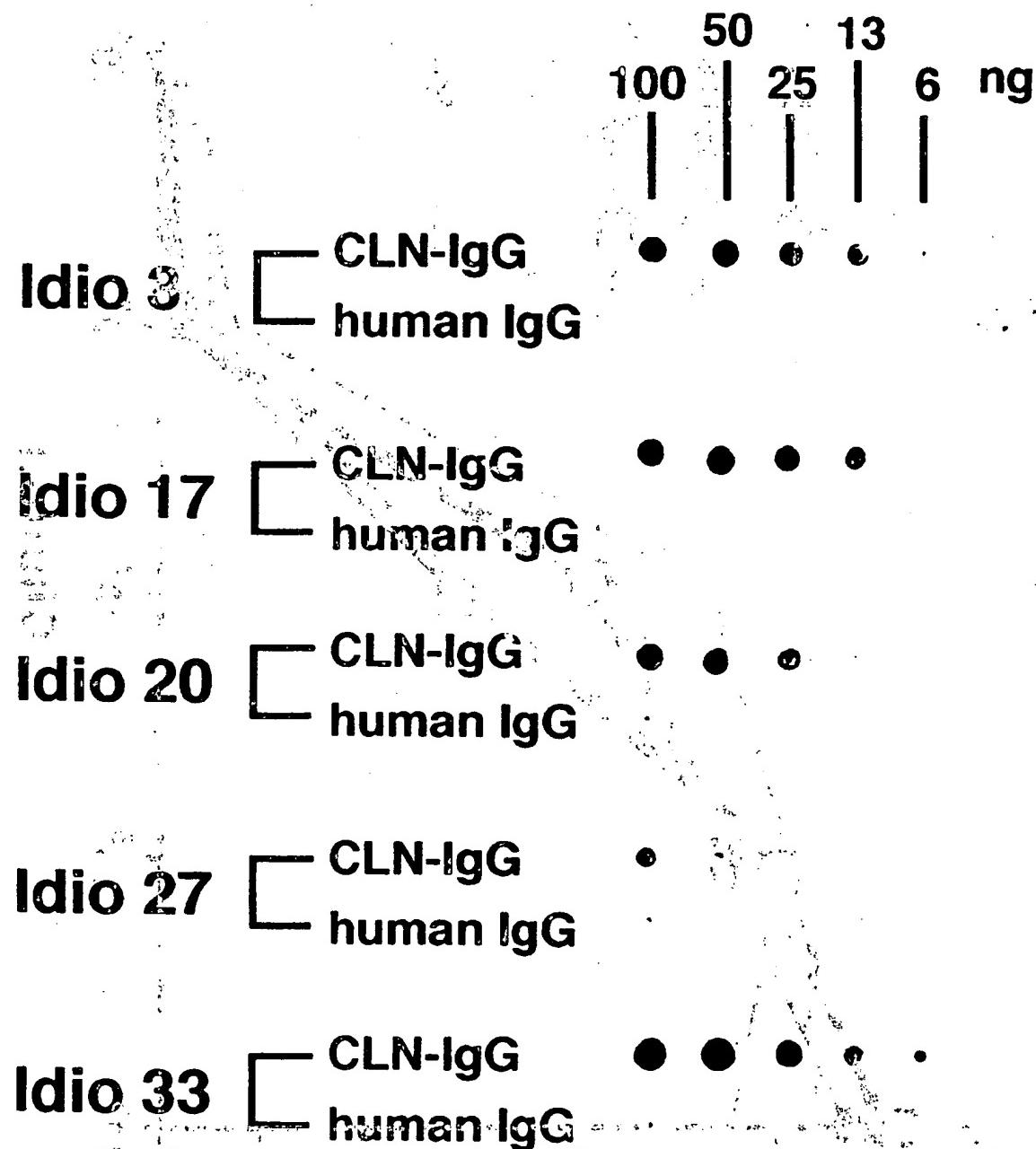


FIG. 3

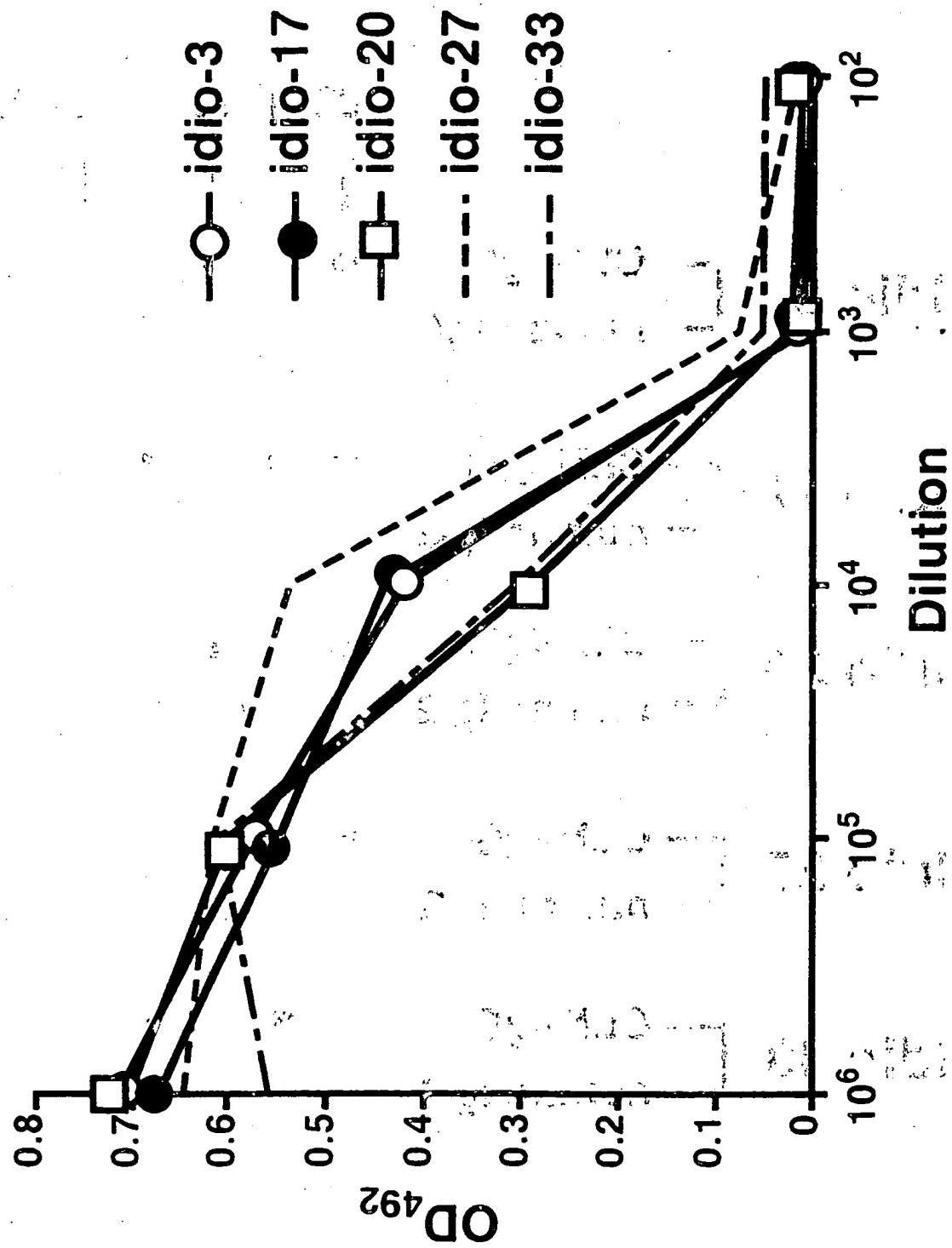


FIG. 4

**3 17 20 27 33**

1	Glu	Glu	Glu	Glu	Glu		68	Lys	Lys	Thr	Thr	Thr	
2	Val	Val	Val	Val	Val		69	Leu	Leu	Ile	Ile	Ile	Leu
3	Gln	Gln	Lys	Lys	Gln		70	Thr	Thr	Ser	Ser	Ser	Thr
4	Leu	Leu	Leu	Leu	Leu		71	Ala	Ala	Arg	Arg	Arg	Ala
5	Gln	Gln	Val	Val	Gln		72	Val	Val	Asp	Asp	Asp	Ala
6	Gln	Gln	Glu	Glu	Gln		73	Thr	Thr	Asn	Asn	Ser	Lys
7	Ser	Ser	Ser	Ser	Ser		74	Ser	Ser	Pro	Ser	Ser	Ser
8	Gly	Gly	Gly	Gly	Gly		75	Thr	Thr	Gln	Gln	Ser	Ser
9	Thr	Thr	Gly	Gly	Ala		76	Ser	Ser	Ser	Ser	Ser	Ser
10	Val	Val	Gly	Gly	Glu		77	Thr	Thr	Ile	Ile	Ile	Thr
11	Leu	Leu	Leu	Leu	Leu		78	Ala	Ala	Leu	Leu	Tyr	Ala
12	Ala	Ala	Val	Val	Ala		79	Tyr	Tyr	Tyr	Tyr	Tyr	Tyr
13	Arg	Arg	Gln	Gln	Arg		80	Met	Met	Ieu	Ieu	Ieu	Met
14	Pro	Pro	Pro	Pro	Pro		81	Glu	Glu	Gln	Gln	Gln	Gln
F	15	Gly	Gly	Gly	Gly		82	Leu	Leu	Met	Met	Met	Leu
A	16	Ala	Ala	Gly	Gly	Ala	82A	Arg	Arg	Asn	Asn	Ser	Ser
1	17	Ser	Ser	Ser	Ser	Ser	82B	Ser	Ser	Thr	Thr	Ser	Ser
18	Val	Val	Leu	Leu	Val	82C	Leu	Leu	Leu	Leu	Leu	Leu	
19	Lys	Lys	Arg	Arg	Asn	83	Thr	Thr	Thr	Arg	Ala		
20	Met	Met	Leu	Leu	Leu	84	Asn	Asn	Thr	Ala	Ser		
21	Ser	Ser	Ser	Ser	Ser	85	Glu	Glu	Glu	Glu	Glu		
22	Cys	Cys	Cys	Cys	Cys	86	Asp	Asp	Asp	Asp	Asp		
23	Lys	Lys	Ala	Ala	Lys	87	Ser	Ser	Ser	Ser	Ser		
24	Ala	Ala	Thr	Thr	Ala	88	Ala	Ala	Ala	Ala	Ala		
25	Ser	Ser	Ser	Ser	Ser	89	Val	Val	Thr	Thr	Val		
26	Gly	Gly	Gly	Gly	Gly	90	Tyr	Tyr	Tyr	Tyr	Tyr		
27	Tyr	Tyr	Leu	Phe	Tyr	91	Phe	Phe	Tyr	Tyr	Tyr		
28	Thr	Thr	Thr	Thr	Thr	92	Cys	Cys	Cys	Cys	Cys		
29	Phe	Phe	Phe	Phe	Phe	93	Thr	Thr	Ala	Ala	Ala		
30	Asn	Asn	Thr	Thr	Thr	94	Lys	Lys	Arg	Arg	Arg		
C	31	Ser	Ser	Asp	Asp	Asn	95	Glu	Glu	Asp	Asp	Ser	
D	32	Tyr	Tyr	Tyr	Tyr	Tyr	96	Glu	Glu	Arg	Gly	Gly	
R	33	Trp	Trp	Tyr	Tyr	Trp	97	Tyr	Tyr	Gly	Phe	Tyr	
1	34	Met	Met	Met	Met	Met	98	Asp	Asp	Gly	Leu	Tyr	
F	35	His	His	Asn	Asn	Gln	99	Tyr	Tyr	Arg	Arg	Gly	
R	36	Trp	Trp	Trp	Trp	Trp	100	Asp	Asp	Asp	Asp	Ser	
2	37	Val	Val	Val	Val	Val	100A	Thr	Thr	---	---	Phe	
F	38	Lys	Tyr	Arg	Arg	Lys	100B	---	---	---	---	Val	
R	39	Gln	Gln	Gln	Gln	Gln	100C	---	---	---	---	Gly	
2	40	Arg	Arg	Pro	Pro	Arg	100D	---	---	---	---	---	
F	41	Pro	Pro	Pro	Pro	Pro	100E	---	---	---	---	---	
R	42	Gly	Gly	Gly	Gly	Gly	100F	---	---	---	---	---	
2	43	Gln	Gln	Lys	Lys	Gln	100G	---	---	---	---	---	
F	44	Gly	Gly	Glu	Ala	Gly	100H	---	---	---	---	---	
R	45	Leu	Leu	Leu	Leu	Leu	100I	---	---	Trp	Trp	---	
2	46	Glu	Glu	Glu	Glu	Glu	100J	---	---	Tyr	Tyr	---	
F	47	Trp	Trp	Trp	Trp	Trp	100K	Leu	Leu	Phe	Phe	Phe	
R	48	Ile	Ile	Leu	Ile	Ile	101	Asp	Asp	Asp	Asp	Ala	
2	49	Gly	Gly	Gly	Gly	Gly	102	Tyr	Tyr	Val	Val	Tyr	
C	50	Ala	Ala	Phe	Phe	Ala	103	Trp	Trp	Trp	Trp	Trp	
D	51	Ile	Ile	Ile	Ile	Ile	104	Gly	Gly	Gly	Gly	Gly	
R	52	Tyr	Tyr	Arg	Arg	Tyr	105	Gln	Gln	Ala	Ala	Gln	
2	53	Pro	Pro	Asn	Asn	Pro	106	Gly	Gly	Gly	Gly	Gly	
F	54	---	---	Lys	Lys	---	107	Thr	Thr	Thr	Thr	Thr	
R	55	---	---	Ala	Ala	---	108	Ser	Ser	Thr	Thr	Leu	
2	56	Gly	Gly	Asn	Asn	Gly	109	Val	Val	Val	Val	Val	
F	57	Asn	Asn	Leu	Tyr	Asp	110	Thr	Thr	Thr	Thr	Thr	
R	58	Ser	Ser	Tyr	Tyr	Gly	111	Val	Val	Val	Val	Val	
2	59	Asp	Asp	Thr	Thr	Asp	112	Ser	Ser	Ser	Ser	Ser	
F	60	Ile	Ile	Thr	Thr	Thr	113	Ser	Ser	Ser	Ser	Ala	
R	61	Ser	Ser	Ser	Ser	Thr							
2	62	Gln	Gln	Ala	Ala	Gln							
F	63	Asn	Asn	Ser	Ser	Lys							
R	64	Phe	Phe	Val	Val	Phe							
2	65	Lys	Lys	Lys	Lys	Lys							
F	66	Asp	Asp	Gly	Gly	Gly							
R	67	Arg	Arg	Arg	Arg	Lys							
2		Ala	Ala	Phe	Phe	Ala							

## FIG. 5

3 17 20 27 33

	1	Asp	Asp	Asp	Asp	Asp	Asp		65	Ser	Ser	Ser	Ser	Ser	Ser	
	2	Ile	Ile	Ile	Ile	Ile	Ile		66	Gly	Gly	Gly	Gly	Gly	Gly	
	3	Val	Val	Val	Val	Val	Val		67	Gly	Ser	Ser	Ser	Ser	Ser	
	4	Leu	Leu	Leu	Met	Met			68	Gly	Gly	Gly	Gly	Gly	Gly	
	5	Thr	Thr	Thr	Thr	Thr			69	Thr	Thr	Thr	Thr	Thr	Thr	
	6	Gln	Gln	Gln	Gln	Gln			70	Asp	Asp	Asp	Asp	Asp	Asp	
	7	Ser	Ser	Ser	Ser	Ser			71	Phe	Phe	Phe	Phe	Phe	Phe	
	8	Pro	Pro	Pro	His	His			72	Thr	Thr	Thr	Thr	Thr	Thr	
	9	Ala	Ala	Ala	Lys	Lys			73	Leu	Leu	Leu	Phe	Phe	Phe	
	10	Ser	Ser	Ser	Phe	Phe			74	Asn	Asn	Asn	Thr	Thr	Thr	
	11	Leu	Leu	Leu	Met	Met			75	Ile	Ile	Ile	Ile	Ile	Ile	
F	12	Ala	Ala	Ala	Ser	Ser			76	His	His	His	Ser	Ser	Ser	
R	13	Val	Val	Val	Thr	Thr			77	Pro	Pro	Pro	Ser	Ser	Ser	
1	14	Ser	Ser	Ser	Ser	Ser			78	Val	Val	Val	Val	Val	Val	
	15	Pro	Leu	Leu	Val	Val			79	Glu	Glu	Glu	Gln	Gln		
	16	Leu	Gly	Gly	Gly	Gly			80	Glu	Glu	Glu	Ala	Ala		
	17	Gly	Gln	Gln	Asp	Asp			81	Glu	Glu	Glu	Glu	Glu		
	18	Gln	Arg	Arg	Arg	Arg			82	Asp	Asp	Asp	Asp	Asp		
	19	Arg	Ala	Ala	Val	Val			83	Ala	Ala	Ala	Leu	Leu		
	20	Ala	Ser	Thr	Ser	Thr			84	Ala	Ala	Ala	Ala	Ala		
	21	Thr	Ile	Ile	Ile	Ile			85	Thr	Thr	Thr	Val	Val		
	22	Ile	Ser	Ser	Thr	Thr			86	Tyr	Tyr	Tyr	Tyr	Tyr		
	23	Ser	---	---	Cys	Cys			87	Tyr	Tyr	Tyr	Tyr	Tyr		
	24	Tyr	Tyr	Tyr	Lys	Lys			88	Cys	Cys	Cys	Cys	Cys		
	25	Arg	Arg	Arg	Ala	Ala			89	Gln	Gln	Gln	Gln	Gln		
	26	Ala	Ala	Ala	Ser	Ser			90	His	His	His	Gln	Gln		
	27	Ser	Ser	Ser	Gln	Gln			91	Ile	Ile	Ile	His	His		
	27A	Lys	Lys	Lys	---	---			92	Arg	Arg	Glu	Tyr	Tyr		
	27B	Ser	Ser	Ser	---	---			93	Val	Gly	Gly	Ser	Ser		
C	27C	Val	Val	Val	---	---			94	Ala	Ala	Pro	Thr			
D	27D	Gln	Ser	Ser	---	---			95	---	---	---	Pro	Ala		
D	27E	Leu	Thr	Thr	---	---			95A	---	---	---	---	---		
R	27F	His	---	---	---	---			95B	---	---	---	---	---		
1	28	Leu	Ser	Ser	Asp	Asp			95C	---	---	---	---	---		
	29	Ala	Gly	Gly	Val	Val			95D	---	---	---	---	---		
	30	Ile	Tyr	Tyr	Asn	Thr			95E	---	---	---	---	---		
	31	Val	Ser	Ser	Thr	Thr			95F	---	---	---	---	---		
	32	Tyr	Tyr	Tyr	Ala	Asp			96	Tyr	Tyr	Tyr	Leu	Trp		
	33	Met	Met	Met	Val	Val			97	Thr	Thr	Thr	Thr	Thr		
	34	His	His	His	Ala	Ala			98	Phe	Phe	Phe	Phe	Phe		
	35	Trp	Trp	Trp	Trp	Trp			99	Gly	Gly	Gly	Gly	Gly		
	36	Asn	Asn	Asn	Tyr	Tyr			F	100	Gly	Gly	Gly	Ala	Gly	
	37	Gln	Gln	Gln	Gln	Gln			R	101	Gly	Gly	Gly	Gly	Gly	
	38	Gln	Gln	Gln	Gln	Gln			102	Thr	Thr	Thr	Thr	Thr		
F	39	Lys	Lys	Arg	Lys	Lys			4	103	Lys	Lys	Lys	Lys		
R	40	Pro	Pro	Pro	Pro	Pro			104	Leu	Leu	Leu	Leu			
2	41	Gly	Gly	Gly	Gly	Arg			105	Glu	Glu	Glu	Glu	Glu		
2	42	Gln	Gln	Gln	Gln	Gln			106	Ile	Ile	Ile	Ile	Ile		
	43	Pro	Pro	Pro	Ser	Ser			107	Lys	Lys	Lys	Lys	Lys		
	44	Pro	Pro	Pro	Pro	Pro										
	45	Arg	Arg	Arg	Lys	Lys										
	46	Leu	Leu	Leu	Leu	Leu										
	47	Leu	Leu	Leu	Leu	Leu										
	48	Ile	Ile	Ile	Ile	Ile										
	49	Tyr	Tyr	Tyr	Tyr	Tyr										
	50	Leu	Leu	Leu	Ser	Ser										
C	51	Val	Val	Val	Ala	Ala										
D	52	Ser	Ser	Ser	Ser	Ser										
D	53	Asn	Asn	Asn	Tyr	Tyr										
R	54	Leu	Leu	Leu	Arg	Arg										
2	55	Glu	Glu	Asp	Tyr	Tyr										
	56	Ser	Ser	Ser	Thr	Thr										
	57	Gly	Gly	Gly	Gly	Gly										
	58	Val	Val	Val	Val	Val										
	59	Pro	Pro	Pro	Pro	Pro										
	60	Ala	Ala	Ala	Asp	Asp										
	61	Arg	Arg	Arg	His	Arg										
	62	Phe	Phe	Phe	Phe	Phe										
	63	Ser	Ser	Ser	Thr	Thr										
	64	Gly	Gly	Gly	Gly	Gly										



European Patent  
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## EUROPEAN SEARCH REPORT

Application Number

EP 94 11 5683

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.)	
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	C12N15/13 C07K16/42	
A	US-A-5 208 146 (R. ERIE) * the whole document * ---	1-27	C12N15/13 C07K16/42	
A	WO-A-89 00050 (AKZO NV) * claims * * examples *	1-27		
A	WO-A-93 10221 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) * the whole document *	1-27		
A	EUROPEAN JOURNAL OF CANCER AND CLINICAL ONCOLOGY, vol.24, no.5, May 1988, OXFORD, GB pages 829 - 838 Y. AOTSUKA ET AL. 'Identification of a malignant cell associated/antigen recognized by a human monoclonal antibody.' * abstract *	1-27		
A	PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE USA, vol.80, no.20, October 1983, WASHINGTON DC, USA pages 6327 - 6331 M. GLASSY ET AL. 'UC 729-6, a human lymphoblastoid B-cell line useful for generating antibody-secreting human-human hybridomas.' * abstract *	1-27	C12N C07K	
-/-				
The present search report has been drawn up for all claims.				
Place of search	Date of completion of the search	Examiner		
THE HAGUE	16-March 1995	Nooij, F		
CATEGORY OF CITED DOCUMENTS				
X : particularly relevant if taken alone	T : theory or principle underlying the invention			
Y : particularly relevant if combined with another document of the same category	E : earlier patent document, but published on, or after the filing date			
A : technological background	D : document cited in the application			
O : non-written disclosure	L : document cited for other reasons			
P : intermediate document	& : member of the same patent family, corresponding document			



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DOCUMENTS CONSIDERED TO BE RELEVANT									
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)						
A	<p><b>CANCER RESEARCH,</b> vol.52, no.9, 1 May 1992, PHILADELPHIA PA, USA pages 2603 - 2609</p> <p>W. TADDEI-PETERS ET AL. 'Quantitation of human tumor-reactive monoclonal antibody 16.88 in the circulation and localization of 16.88 in colorectal metastatic tumor tissue using murine antiidiotypic antibodies.'</p> <p>* abstract *</p>	1-27	10-08-1-38 22020 22111X5						
P,A	<p><b>MOLECULAR IMMUNOLOGY,</b> vol.30, no.16, November 1993, OXFORD, GB pages 1481 - 1489</p> <p>K. YAGO ET AL. 'Immunoglobulin variable region sequences of two human monoclonal antibodies directed to an onco-developmental carbohydrate antigen, lactotetraosylceramide (LcOse4Cer).'</p> <p>* abstract *</p>	1-27	10-08-1-38 22020 22111X5						
<p>The present search report has been drawn up for all claims.</p> <table border="1"> <tr> <td>Place of search</td> <td>Date of compilation of the search</td> <td>Examiner</td> </tr> <tr> <td>THE HAGUE</td> <td>16 March 1995</td> <td>Nooij, F.</td> </tr> </table>				Place of search	Date of compilation of the search	Examiner	THE HAGUE	16 March 1995	Nooij, F.
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THE HAGUE	16 March 1995	Nooij, F.							
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: non-written disclosure	L : document cited for other reasons								
P : intermediate document	R : member of the same patent family, corresponding document								

4000' 1000' 500' 250' 100' 50' 25' 10' 5'

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4000' 2000' 1000' 500' 250' 100' 50' 25' 10' 5'

8000' 4000' 2000' 1000' 500' 250' 100' 50' 25' 10' 5'

16000' 8000' 4000' 2000' 1000' 500' 250' 100' 50' 25' 10' 5'

32000' 16000' 8000' 4000' 2000' 1000' 500' 250' 100' 50' 25' 10' 5'

64000' 32000' 16000' 8000' 4000' 2000' 1000' 500' 250' 100' 50' 25' 10' 5'

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256000' 128000' 64000' 32000' 16000' 8000' 4000' 2000' 1000' 500' 250' 100' 50' 25' 10' 5'

512000' 256000' 128000' 64000' 32000' 16000' 8000' 4000' 2000' 1000' 500' 250' 100' 50' 25' 10' 5'

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